

chain nodes :

25 26 28 29 34

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
22 23

chain bonds :

4-18 15-34 25-26 25-28 28-29

ring bonds :

1-2 1-7 1-13 2-3 2-8 3-4 3-10 4-5 5-6 6-7 7-11 8-9 9-10 9-14
10-17 11-12 12-13 14-15 15-16 16-17 18-19 18-23 19-20 20-21
21-22 22-23

exact/norm bonds :

1-2 1-7 1-13 2-3 2-8 3-4 3-10 4-5 5-6 6-7 7-11 8-9 9-10 9-14
10-17 11-12 12-13 14-15 15-16 15-34 16-17 25-26 25-28 28-29

exact bonds :

4-18

normalized bonds :

18-19 18-23 19-20 20-21 21-22 22-23

isolated ring systems :

containing 18 :

G1:O,S

G2:H, [*1]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom
18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 25:CLASS 26:CLASS
28:CLASS 29:Atom 34:CLASS

09/701,893

=> d his

(FILE 'HOME' ENTERED AT 12:32:08 ON 21 NOV 2001)

FILE 'REGISTRY' ENTERED AT 12:32:20 ON 21 NOV 2001

L1 STRUCTURE UPLOADED

L2 QUE L1

L3 19 S L2

L4 425 S L2 SSS FUL

FILE 'CAPLUS' ENTERED AT 12:34:05 ON 21 NOV 2001

L5 130 S L4

FILE 'REGISTRY' ENTERED AT 12:35:30 ON 21 NOV 2001

L6 STRUCTURE UPLOADED

L7 QUE L6

L8 419 S L7 SUB=L4 FUL

FILE 'CAPLUS' ENTERED AT 12:37:01 ON 21 NOV 2001

L9 129 S L8

FILE 'STNGUIDE' ENTERED AT 12:39:27 ON 21 NOV 2001

FILE 'REGISTRY' ENTERED AT 12:42:03 ON 21 NOV 2001

L10 STRUCTURE UPLOADED

L11 QUE L10

L12 14 S L11

L13 14 S L12 SUB=L4 SAM

L14 315 S L12 SUB=L4 FUL

FILE 'CAPLUS' ENTERED AT 12:44:12 ON 21 NOV 2001

L15 124 S L14

L16 ANALYZE L15 1- RN : 1812 TERMS

FILE 'REGISTRY' ENTERED AT 12:45:08 ON 21 NOV 2001

L17 1 S 65154-06-5/RN

SET NOTICE 1 DISPLAY

SET NOTICE LOGIN DISPLAY

L18 315 S L14 NOT L17

FILE 'REGISTRY' ENTERED AT 12:46:20 ON 21 NOV 2001

L19 1 S 128672-07-1/RN

SET NOTICE 1 DISPLAY

SET NOTICE LOGIN DISPLAY

L20 314 S L14 NOT L19

FILE 'CAPLUS' ENTERED AT 12:47:37 ON 21 NOV 2001

L21 92 S L20

L22 11 S L19 AND L21

L23 92 S L21 OR L22

FILE 'REGISTRY' ENTERED AT 12:48:36 ON 21 NOV 2001

FILE 'CAPLUS' ENTERED AT 12:48:39 ON 21 NOV 2001

=> d bib abs hitstr 123 1-92

09/701,893

~~LES~~ ANSWER 1 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 2001:614326 CAPLUS
DN 135:175426
TI Use of platelet activating factor antagonists as anti-pruritic agents
IN Woodward, David F.; Williams, Linda Sue
PA Allergan Sales, Inc., USA
SO U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 837,568, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6277846	B1	20010821	US 1998-138967	19980824
PRAI	US 1990-530739	B1	19900531		
	US 1992-837568	B2	19920218		

AB The invention relates to a method for treating pruritus by administering a therapeutically effective amt. of a PAF antagonist to a mammal afflicted with pruritus. The PAF antagonists may, for example, be selected from synthetic PAF analogs, natural products isolated from plants having PAF antagonist activity, and triazolobenzodiazepines. The PAF antagonists are preferably applied topically to the afflicted site but systemic such as oral, parenteral, nasal and intrarectal administration, is also possible.

IT **131614-02-3**, E-6123

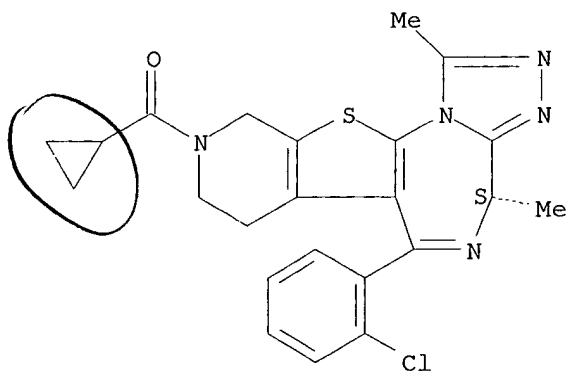
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of platelet activating factor antagonists as anti-pruritic agents)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 30

RE

(1) Anon; EP 0157609 1985 CAPLUS
(2) Anon; WO 8910143 1989 CAPLUS
(3) Anon; WO 9118608 1991 CAPLUS
(5) Billah; US 5334592 1994 CAPLUS
(7) Braquet; US 4734280 1988 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/701,893

123 ANSWER 2 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 2001:167792 CAPLUS

DN 134:227363

TI Topical use of kappa opioid agonists to treat otic pain

IN Gamache, Daniel A.; Yanni, John M.

PA Alcon Laboratories, Inc., USA

SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001015678	A2	20010308	WO 2000-US22766	20000818
	W: AU, BR, CA, CN, JP, MX, PL, TR, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRAI US 1999-387359 A 19990831

AB Topical or intranasal compns. and methods for treating otic pain caused by otitis, surgery, or swimmer's ear are disclosed. In particular, the invention discloses compns. and methods of using .kappa.-opioid agonists locally for the prevention or alleviation of otic pain. Compns. also comprise antimicrobial, antiallergy, and anti-inflammatory agents to treat otic infections, allergies, and inflammations assocd. with otic pain. For example, an otic/nasal soln. contained (by wt.) a .kappa.-opioid EMD-61753 0.01-1.0%, phosphate buffered saline 1.0%, Polysorbate 80 0.5%, and water up to 100%.

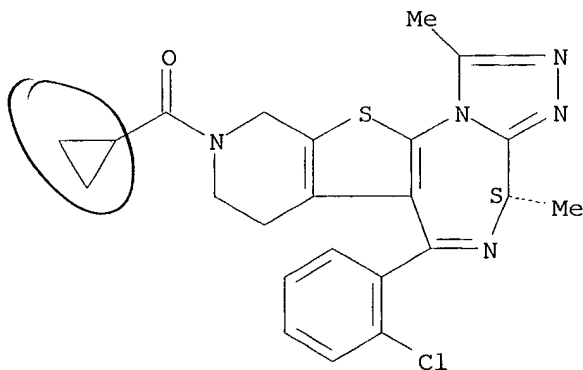
IT 131614-02-3, E-6123 132418-35-0, BN-50727

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical compns. contg. .kappa.-opioid agonists for treatment of otic pain)

RN 131614-02-3 CAPLUS

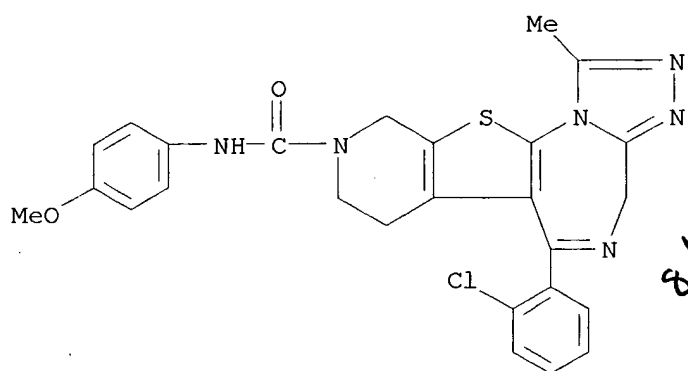
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



8/31/99
not prior art

~~133~~ ANSWER 3 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 2001:167791 CAPLUS

DN 134:227362

TI Use of 5-HT1B/1D agonists to treat otic pain

IN Gamache, Daniel A.; Yanni, John M.; Sharif, Najam A.

PA Alcon Laboratories, Inc., USA

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001015677	A2	20010308	WO 2000-US22764	20000818
	W: AU, BR, CA, CN, JP, MX, PL, TR, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRAI US 1999-387358 **ABN** A 19990831

AB Topical otic or intranasal compns. and methods for treating otic pain caused by otitis, surgery, or swimmer's ear are disclosed. In particular, the invention discloses compns. and methods of using 5-HT1B/1D agonists for the prevention or alleviation of otic pain. Compns. also comprise an antimicrobial, antiallergy, and anti-inflammatory agent to treat otic infections, allergies, and inflammations assocd. with otic pain. For example, an otic/nasal soln. contained CGS-12066A 0.01-1.0%, phosphate buffered saline 1.0%, Polysorbate 80 0.5%, and water up to 100% (wt./vol.), resp.

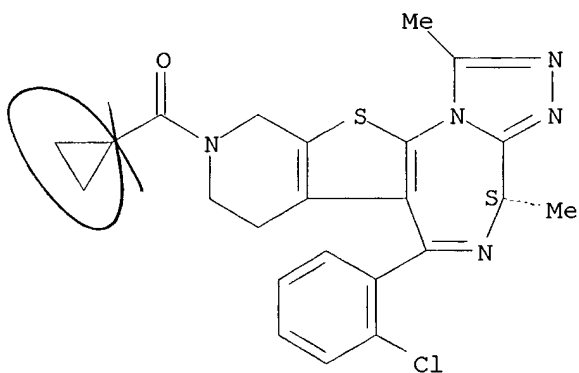
IT **131614-02-3**, E-6123 **132418-35-0**, BN-50727

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical compns. of 5-HT1B/1D agonists for treatment of otic pain)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

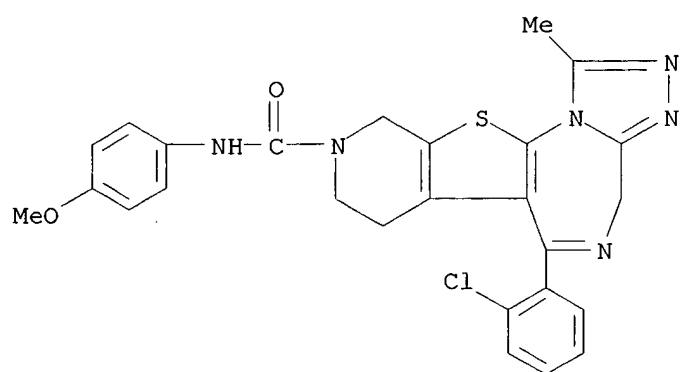
Absolute stereochemistry.



RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



✓
 123 ANSWER 4 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 2001:161904 CAPLUS

DN 134:177247

TI Role of phospholipid metabolites in .beta.2-integrin-dependent adhesion of human neutrophils following with IL-8 stimulation

AU Watanabe, Masanari; Sano, Hiroyuki; Tomita, Katsuyuki

CS Third Dep. Intern. Med., Fac. Med., Tottori Univ., Yonago, 683-8504, Japan

SO Yonago Igaku Zasshi (2001), 52(1), 9-20

CODEN: YOIZA3; ISSN: 0044-0558

PB Yonago Igakkai

DT Journal

LA Japanese

AB Chronic obstructive pulmonary disease (COPD) is defined as disease state characterized by the presence of airflow obstruction ue to chronic bronchitis or emphysema. It has been reported that neutrophil counts and interleukin-8 (IL-8) concns. are elevated in bronchoalveolar lavage from patients with COPD. It seems that neutrophil and IL-8 play key roles in the development of COPD. We examd. the role of arachidonic metabolites in IL-8-stimulated neutrophil adhesion to a counterligand contained in bovine serum albumin (BSA). We first confirmed that neutrophil adhesion to BSA-coated plate was .beta.2-integrin dependent. IL-8 induced neutrophil adhesion to BSA time- and concn.-dependently. Neutrophil adhesion was significantly elevated at 30 nM of IL-8 for 30 min (26.6 .+- . 3.1% vs. 6.0 .+- . 1.2% in control; p <0.01). Preincubation of neutrophil with E6123, platelet activating factor (PAF) receptor antagonist, blocked IL-8-induced neutrophil adhesion to BSA concn.-dependently. At 30 .mu.M, E6123 blocked the adhesion to 51.9 .+- . 5.8% of control (p <0.01). In contrast, neutrophil adhesion was unchanged in the presence of AA-861 (lipoxygenase (5-LO) inhibitor) or indomethacin (cyclooxygenase (COX) inhibitor). Moreover, exogenous PAF also induced neutrophil adhesion to BSA time- and concn.-dependently, while lysoPAF had no effect. On the surface adhesion mols. expression, IL-8 enhanced CD11b expression but neither CD11a nor CD11c. IL-8-enhanced CD11b expression on neutrophils was partially suppressed with 30 .mu.M of E6123 (110 .+- . 4.5 mean fluorescence intensity (MFI) vs. 148.9 .+- . 3.7 MFI in control; p <0.05). These results suggest that endogenous PAF induced by IL-8 may play an important role in neutrophil-.beta.2-dependent adhesion.

IT 131614-02-3, E6123

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

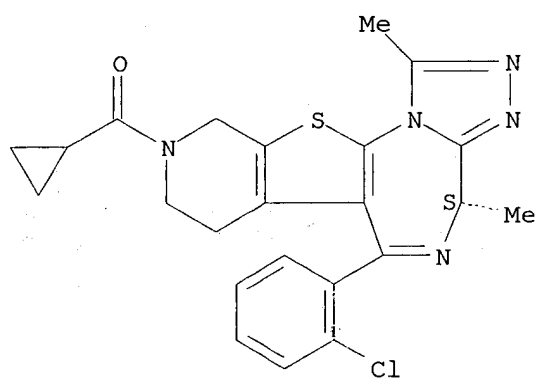
(arachidonate metabolites no relation to IL-8-induced .beta.2-integrin-dependent adhesion of neutrophils in humans with chronic obstructive pulmonary disease)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



09/701,893

~~123~~ ANSWER 5 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 2000:636335 CAPLUS

DN 133:206699

TI The role of lipid mediators in bronchial hyperresponsiveness and airway eosinophil accumulation induced by antigen challenge in guinea pigs

AU Tachibana, Hideki

CS The 3rd Dep. Intern. Med., Kanazawa Univ. Sch. Med., Japan

SO Arerugi (2000), 49(8), 634-645

CODEN: ARERAM; ISSN: 0021-4884

PB Nippon Arerugi Gakkai

DT Journal

LA Japanese

AB The aim of this study was elucidate the role of lipid mediators in bronchial hyperresponsiveness (BHR) and airway eosinophil accumulation 24 h after an antigen challenge in guinea pigs. Thromboxane (TX) A2 receptor antagonist, S-1452 (1, 10 mg/kg), cysteinyl leukotriene (CLT) receptor antagonist, ICI-198,615 (0.5, 5 mg/kg), platelet activating factor (PAF) receptor antagonist, E-6123 (1,10 .mu.g/kg), and each vehicle were i.p. given 1 h before and 11 h after an ovalbumin (OVA) challenge. BHR to inhaled methacholine was measured and then bronchoalveolar lavage (BAL) was performed 24 h after the OVA challenge. The three drugs significantly inhibited BHR to methacholine, dose dependently. S-1452 significantly inhibited total cell counts (TCC), ICI-198,615 significantly reduced both TCC and eosinophil percentage, but E-6123 did not alter TCC and cell differentiation in BAL fluid. Therefore, these results clearly showed that lipid mediators were involved in antigen-induced BHR and suggested that TXA2 and CLT may contribute to the penetration of inflammatory cells through capillary wall, still more CLT is concerned eosinophil accumulation with cell specificity. PAF dose not take part in the penetration of inflammatory cells.

IT 131614-02-3, E 6123

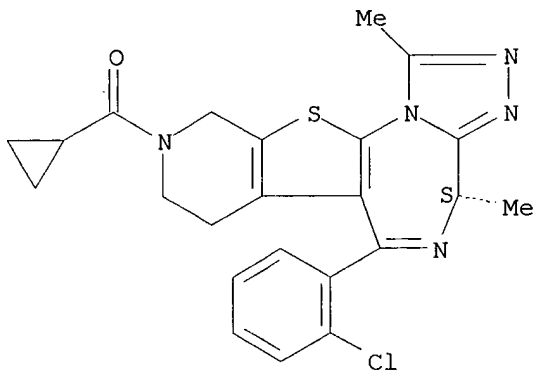
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(role of lipid mediators in bronchial hyperresponsiveness and its treatment)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

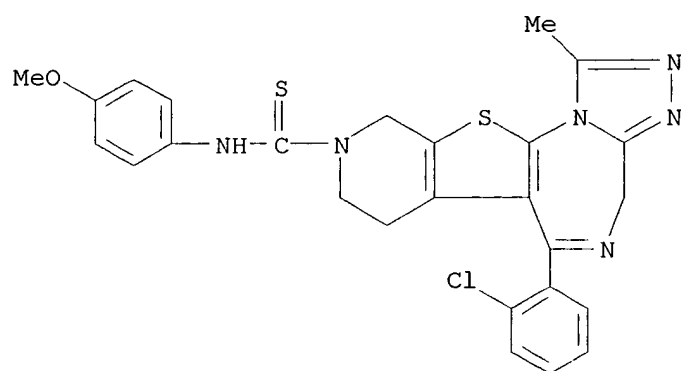
Absolute stereochemistry.



09/701,893

✓
 LPS ANSWER 6 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 2000:447253 CAPLUS
 DN 133:174994
 TI Platelet activating factor (PAF) antagonists on cytokine induction of iNOS and sPLA2 in immortalized astrocytes (DITNC)
 AU Wang, Jing-Hung; Sun, Grace Y.
 CS Nutritional Sciences Program and Biochemistry Department, University of Missouri, Columbia, MO, 65212, USA
 SO Neurochem. Res. (2000), 25(5), 613-619
 CODEN: NEREDZ; ISSN: 0364-3190
 PB Kluwer Academic/Plenum Publishers
 DT Journal
 LA English
 AB Platelet-activating factor (PAF, 1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine) and its receptor are known to play important roles in modulating neuronal plasticity and inflammatory responses, particularly during neuronal injury. PAF receptors are widespread in different brain regions and are present on the cell surface as well as in intracellular membrane compartments. Astrocytes are immune active cells and are responsive to cytokines, which stimulate signaling cascades leading to transcriptional activation of genes and protein synthesis. Our recent studies indicate the ability of cytokines, e.g., tumor necrosis factor- α . (TNF. α .), interleukin-1. β . (IL-1. β .) and interferon- γ . (IFN. γ .), to induce the inducible nitric oxide (iNOS) and secretory phospholipase A2 (sPLA2) genes in immortalized astrocytes (DITNC). The main objective for this study is to examine the effects of PAF antagonists on cytokine induction of iNOS and sPLA2 in these cells. Results show that BN50730, a synthetic PAF antagonist, but not BN52021, a natural PAF antagonist (ginkgolide B) can dose-dependently inhibit cytokine induction of NO prodn. and sPLA2 release. Inhibition of NO prodn. by BN50730 corroborated well with the decrease in iNOS protein and mRNA levels as well as binding of NF- κ .B and STAT-1 to DNA, suggesting that BN50730 action is upstream of the transcriptional process. These results are in agreement with the role of intracellular PAF in regulating the cytokine signaling cascade in astrocytes and further suggest the possible use of BN50730 as a therapeutic agent for suppressing the inflammatory pathways elicited by cytokines.
 IT **132579-32-9**, BN50730
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of platelet activating factor antagonists on cytokine induction of iNOS and sPLA2 in immortalized astrocytes and on NF- κ .B and STAT-1 binding to DNA)
 RN 132579-32-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893

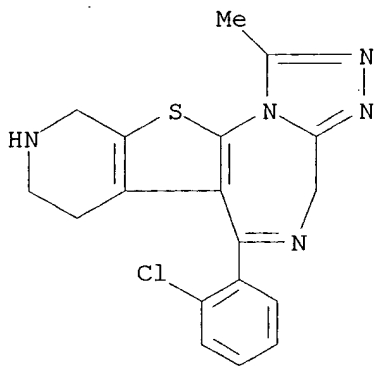


RE.CNT 31

RE

- (1) Bazan, N; Neurochem Int 1995, V26, P435 CAPLUS
 - (2) Bazan, N; Neurochem Int 1997, V30, P225 CAPLUS
 - (3) Bazan, N; Progress Brain Res 1998, V118, P281 CAPLUS
 - (4) Bito, H; J Lipid Mediators 1993, V6, P169 CAPLUS
 - (5) Bussolino, F; Neurochem Int 1995, V26, P425 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~L28~~ ANSWER 7 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 2000:211400 CAPLUS
 DN 132:334372
 TI Isolation and structural data of the opened ring derivative of a
 1,2,4-triazolothieno-1,4-diazepine
 AU Legouin, Beatrice; Burgot, Jean-Louis
 CS U.F.R. des Sciences Pharmaceutiques et Biologiques, Department d'Etudes
 Physicochimiques et Biocinetiques des Pharmacosystemes, Laboratoire de
 Chimie Analytique, Rennes, 35043, Fr.
 SO J. Heterocycl. Chem. (2000), 37(1), 127-129
 CODEN: JHTCAD; ISSN: 0022-152X
 PB HeteroCorporation
 DT Journal
 LA English
 OS CASREACT 132:334372
 AB The prepn. of the trihydrochloride form of 2-[3-(aminomethyl)-5-methyl-
 1,2,4-triazol-4-yl]-3-(2-chlorobenzoyl)thieno[2,3-c]-4,5,6,7-
 tetrahydropyridine was prepd. as the opened deriv. of a
 1,2,4-triazolothieno-1,4-diazepine. Its structural properties are given,
 and are compared with those of the corresponding closed form
 4H-6-(2-chlorophenyl)-1-methyl-7,8,9,10-tetrahydropyrido[4',3':4,5]thieno[
 3,2-f]-[1,2,4]triazolo[4,3-a][1,4]diazepine.
 IT **114800-58-7**
 RL: RCT (Reactant)
 (ring opening of triazolothienodiazepine deriv.)
 RN 114800-58-7 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RE.CNT 20

RE

- (1) Gallo, B; J Heterocyclic Chem 1988, V25, P867 CAPLUS
 - (2) Gallo, B; Pharmazie 1988, V43, P212 CAPLUS
 - (4) Inotsume, N; Chem Pharm Bull 1980, V28, P2536 CAPLUS
 - (5) Jimenez, R; J Heterocyclic Chem 1987, V24, P421 CAPLUS
 - (6) Konishi, M; J Pharm Sci 1982, V71, P1328 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

applicants

L23 ANSWER 8 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1999:811253 CAPLUS

DN 132:49986

TI Use of diazepines for preparing medicines for treating pathological conditions or diseases involving one of the growth hormone release inhibiting factor receptors

IN Bigg, Dennis; Liberatore, Anne-Marie; Pommier, Jacques; Taylor, John

PA Societe De Conseils De Recherches Et D'Applications Scientifiques (S.C.R.A.S, Fr.

SO PCT Int. Appl., 65 pp.

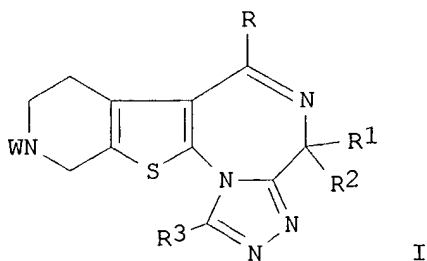
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9965917	A1	19991223	WO 1999-FR1422	19990615
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2779652	A1	19991217	FR 1998-7509	19980615
	FR 2779652	B1	20010608		
	AU 9941495	A1	20000105	AU 1999-41495	19990615
	EP 1087978	A1	20010404	EP 1999-925093	19990615
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NO 2000006352	A	20001213	NO 2000-6352	20001213
PRAI	FR 1998-7509	A	19980615		
	WO 1999-FR1422	W	19990615		
OS	MARPAT 132:49986				
GI					



AB Pyridothienotriazolodiazepines I [W = H, acyl, thioacyl; R = (un)substituted Ph; R1, R2 = H, (un)substituted alkyl, alkenyl, alkynyl; R3 = H, halo, NO2, Cn, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl] were prepd. for use in a medicine for treating pathol. conditions or diseases involving one of the growth hormone release inhibiting factor receptors (no data). Thus, 5-(2-chlorophenyl)-8-ethoxycarbonyl-6,7,8,9-tetrahydro-3H-

pyrido[4,3':4,5]thieno[3,2-e][1,4]diazepine-2-thione was treated with N₂H₄, cyclized to the triazole with BuC(OMe)₃, and decarboxylated to give I [R = 2-ClC₆H₄, R₁, R₂, W = H, R₃ = Bu].

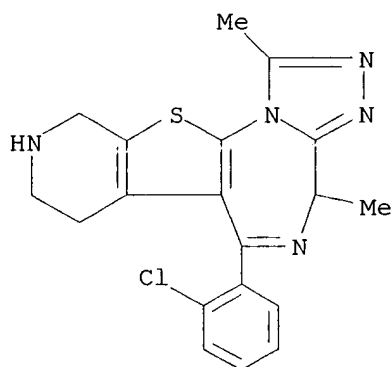
IT **130311-75-0**

RL: RCT (Reactant)

(prepn. of pyridothienotriazolodiazepines as somatostatin antagonists)

RN 130311-75-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX NAME)



IT **114800-58-7P 252754-34-0P 252754-62-4P**

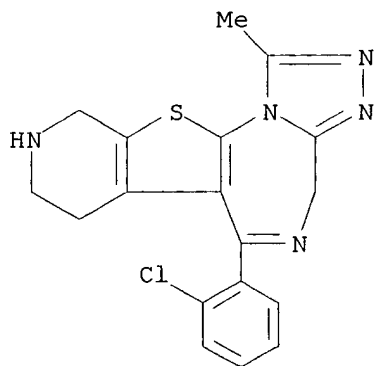
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyridothienotriazolodiazepines as somatostatin antagonists)

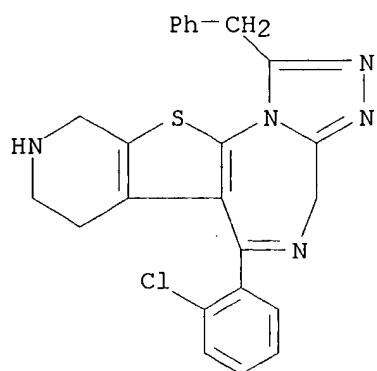
RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



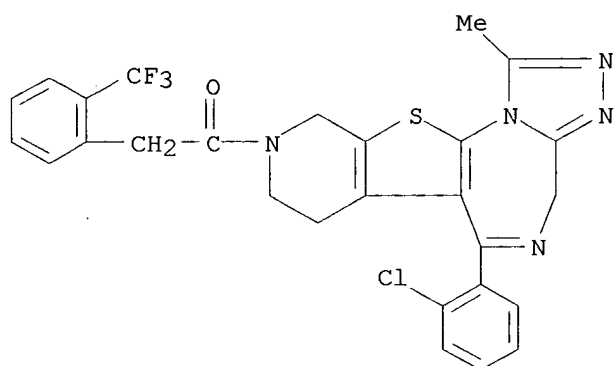
RN 252754-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 252754-62-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[2-(trifluoromethyl)phenyl]acetyl]- (9CI) (CA INDEX NAME)



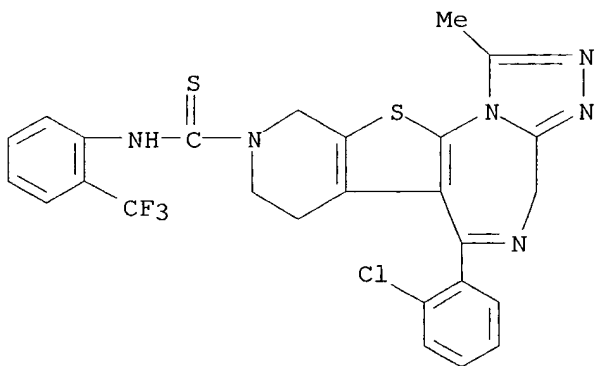
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 252755-76-3P 252755-80-9P 252879-75-7P
 252879-76-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of pyridothienotriazolodiazepines as somatostatin antagonists)

RN 132418-41-8 CAPLUS

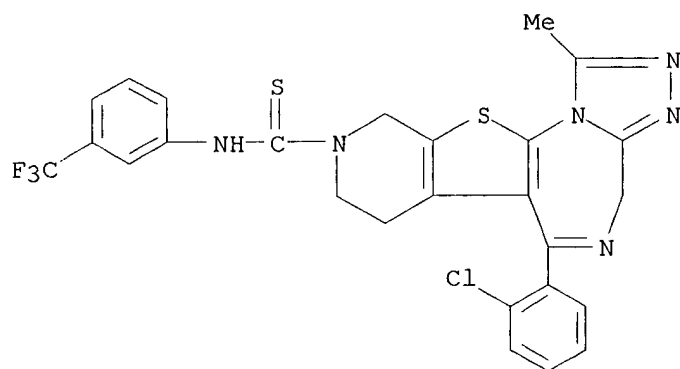
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 132418-42-9 CAPLUS

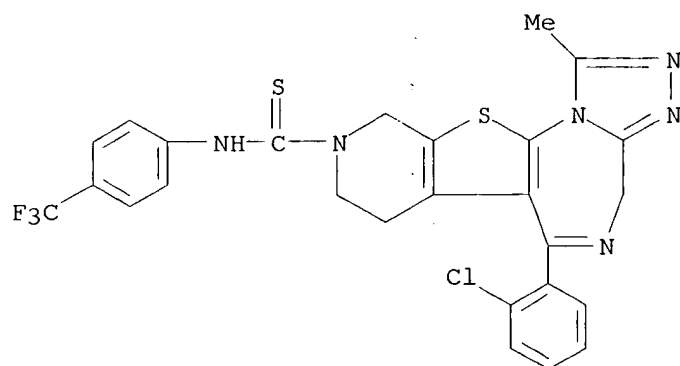
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

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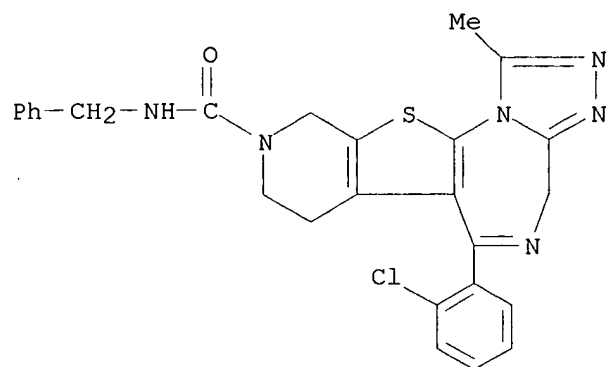
RN 132418-44-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 132418-52-1 CAPLUS

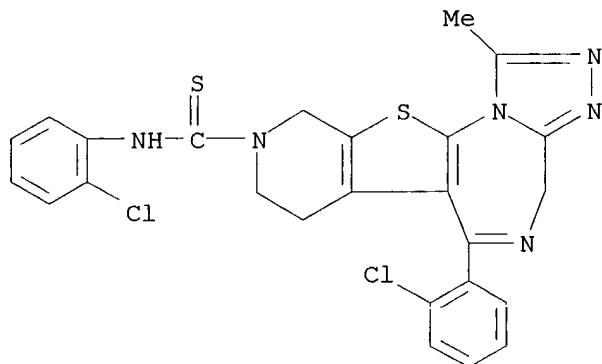
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



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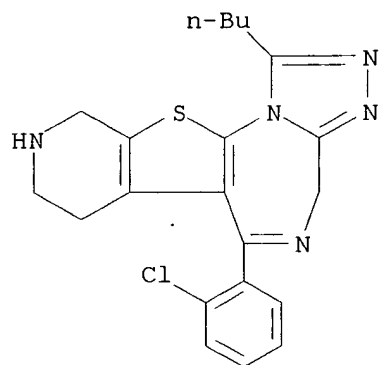
RN 139307-99-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, N,6-bis(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI)
(CA INDEX NAME)



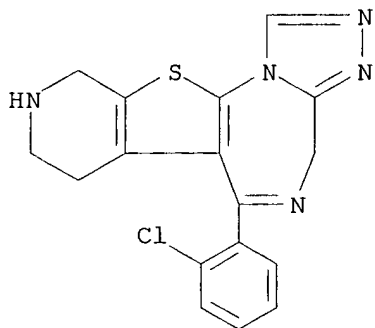
RN 252754-33-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
1-butyl-6-(2-chlorophenyl)-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)



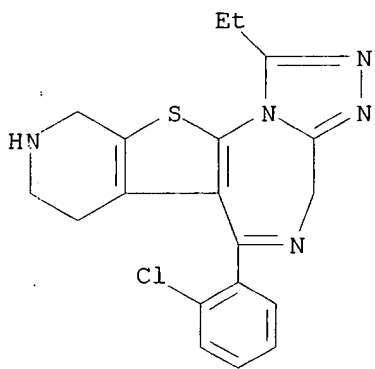
RN 252754-35-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)



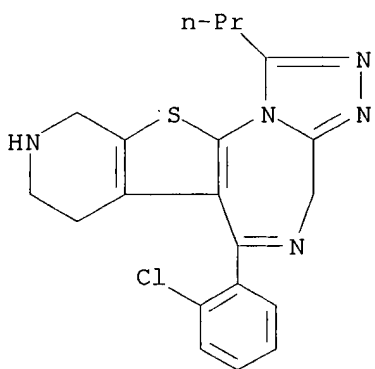
RN 252754-36-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-1-ethyl-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)



RN 252754-37-3 CAPLUS

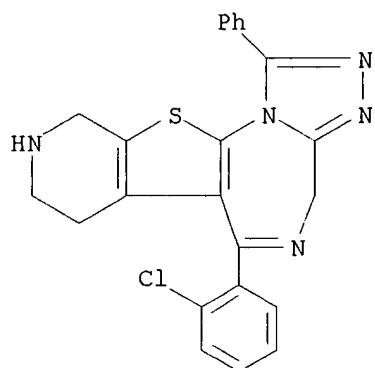
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-propyl- (9CI) (CA INDEX NAME)



RN 252754-38-4 CAPLUS

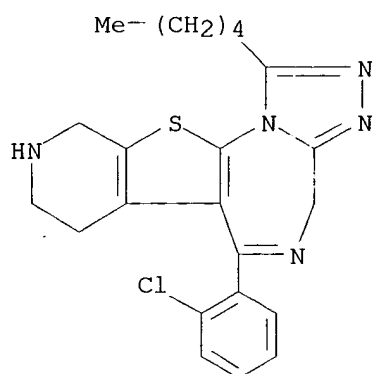
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-phenyl- (9CI) (CA INDEX NAME)

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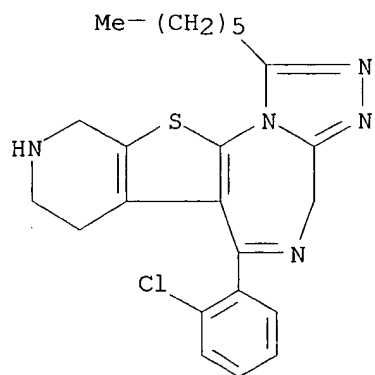
RN 252754-39-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-pentyl- (9CI) (CA INDEX NAME)



RN 252754-40-8 CAPLUS

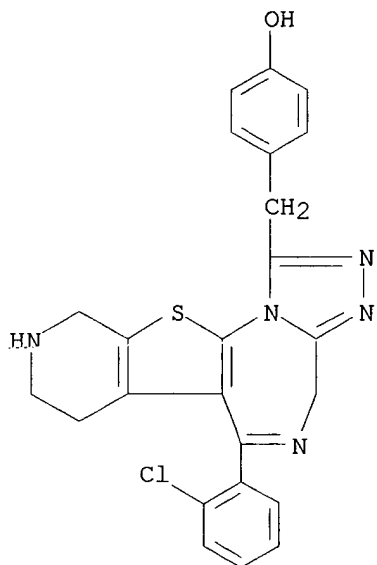
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-1-hexyl-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)



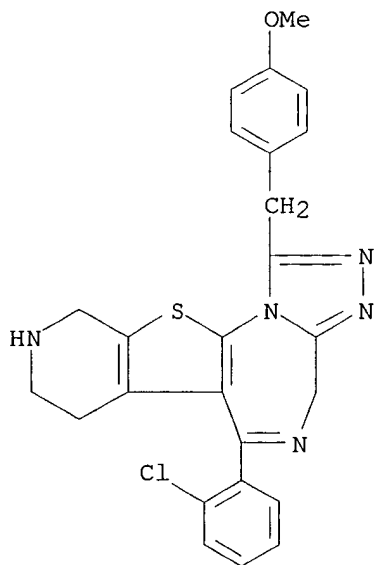
RN 252754-41-9 CAPLUS

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CN Phenol, 4-[[6-(2-chlorophenyl)-7,8,9,10-tetrahydro-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-1-yl)methyl]- (9CI) (CA INDEX NAME)



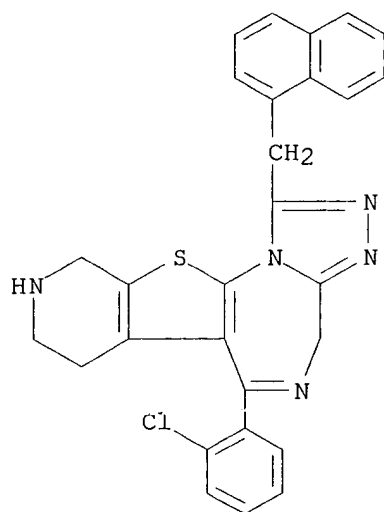
RN 252754-42-0 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-[(4-methoxyphenyl)methyl]- (9CI)
(CA INDEX NAME)



RN 252754-43-1 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-(1-naphthalenylmethyl)- (9CI)

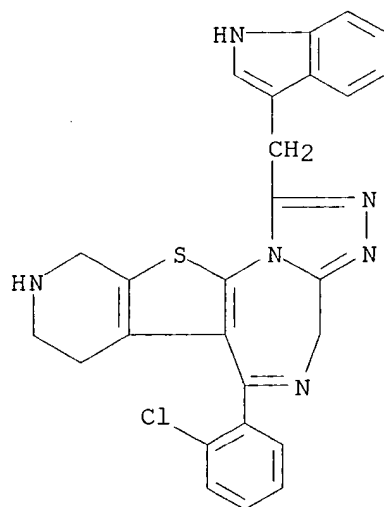
09/701,893

(CA INDEX NAME)



RN 252754-44-2 CAPLUS

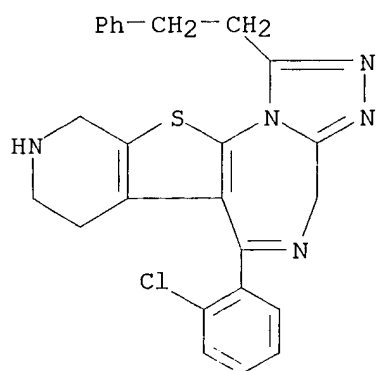
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-(1H-indol-3-ylmethyl)- (9CI) (CA
INDEX NAME)



RN 252754-45-3 CAPLUS

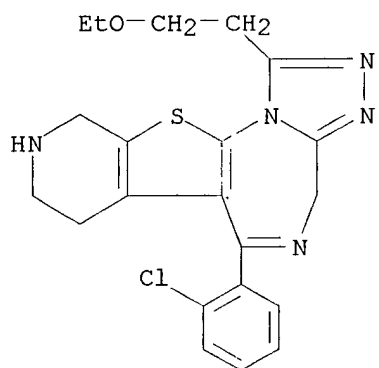
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-(2-phenylethyl)- (9CI) (CA INDEX
NAME)

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RN 252754-46-4 CAPLUS

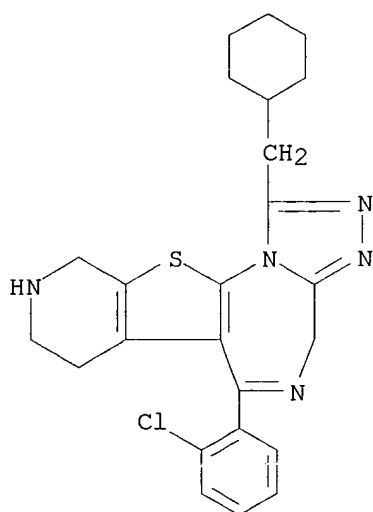
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-1-(2-ethoxyethyl)-7,8,9,10-tetrahydro- (9CI) (CA INDEX
NAME)



RN 252754-47-5 CAPLUS

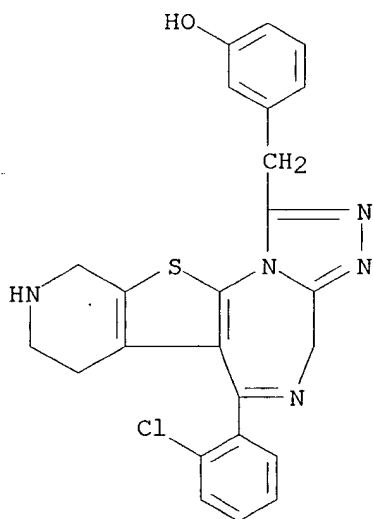
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-1-(cyclohexylmethyl)-7,8,9,10-tetrahydro- (9CI) (CA
INDEX NAME)

09/701,893



RN 252754-48-6 CAPLUS

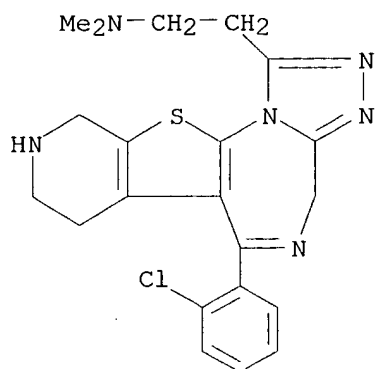
CN Phenol, 3-[[6-(2-chlorophenyl)-7,8,9,10-tetrahydro-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-1-yl]methyl]- (9CI) (CA INDEX NAME)



RN 252754-49-7 CAPLUS

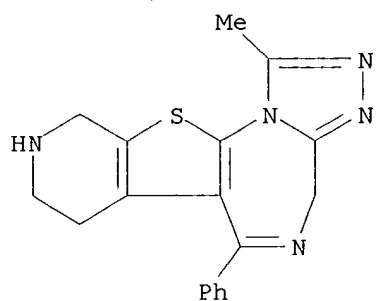
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-1-ethanamine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

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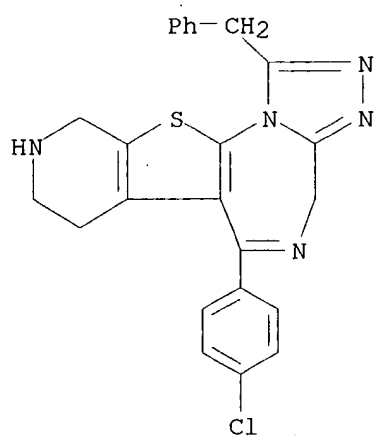
RN 252754-50-0 CAPLUS

4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
7,8,9,10-tetrahydro-1-methyl-6-phenyl- (9CI) (CA INDEX NAME)



RN 252754-51-1 CAPLUS

4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(4-chlorophenyl)-7,8,9,10-tetrahydro-1-(phenylmethyl)- (9CI) (CA INDEX
NAME)

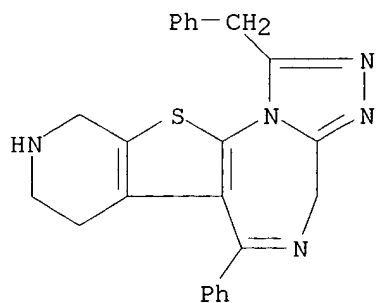


RN 252754-52-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,

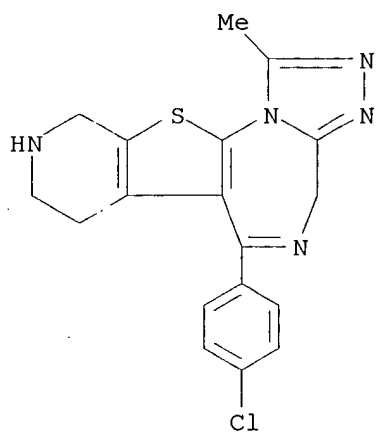
09/701,893

7,8,9,10-tetrahydro-6-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



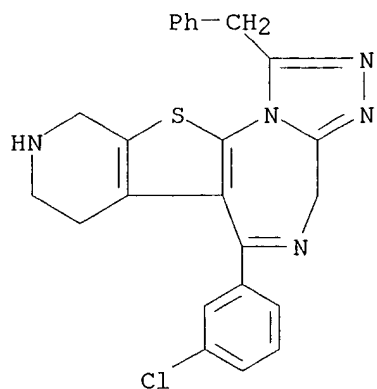
RN 252754-53-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(4-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-54-4 CAPLUS

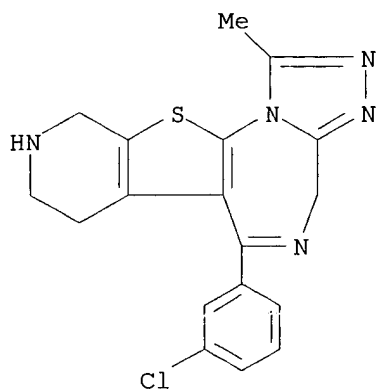
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(3-chlorophenyl)-7,8,9,10-tetrahydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



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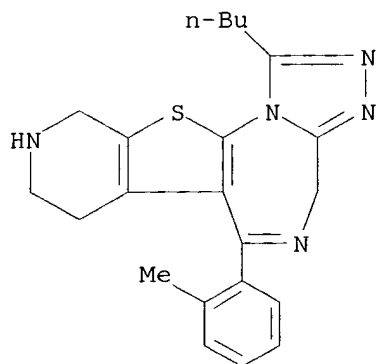
RN 252754-55-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(3-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-56-6 CAPLUS

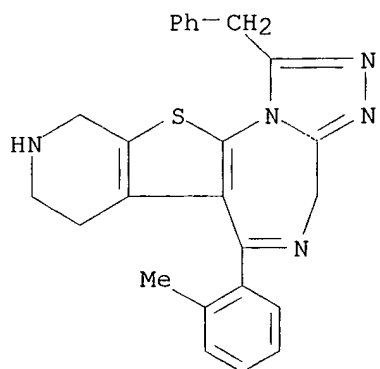
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
1-butyl-7,8,9,10-tetrahydro-6-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 252754-57-7 CAPLUS

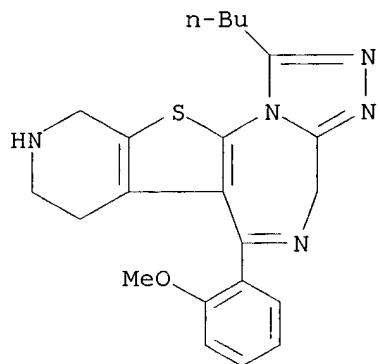
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
7,8,9,10-tetrahydro-6-(2-methylphenyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

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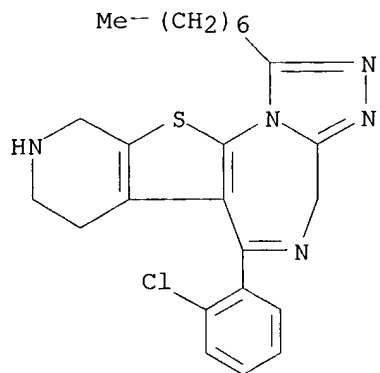
RN 252754-58-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
1-butyl-7,8,9,10-tetrahydro-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252754-59-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-1-heptyl-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)

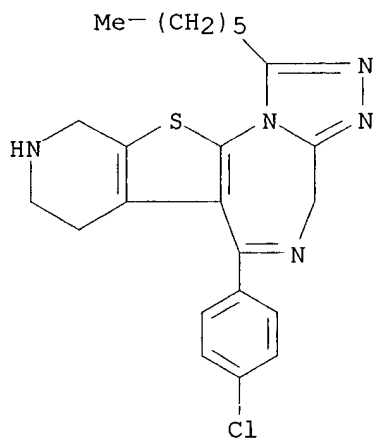


RN 252754-60-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,

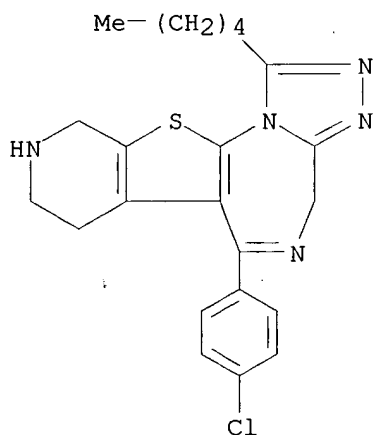
09/701,893

6-(4-chlorophenyl)-1-hexyl-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)



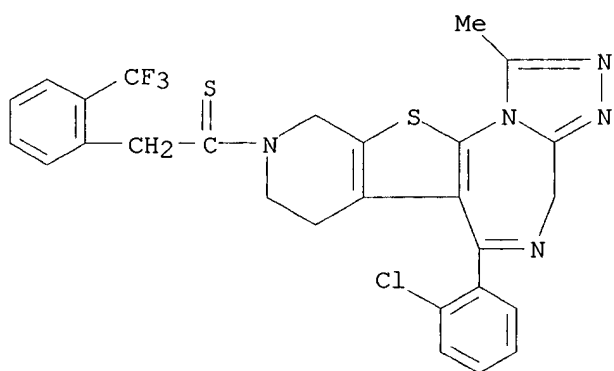
RN 252754-61-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(4-chlorophenyl)-7,8,9,10-tetrahydro-1-pentyl- (9CI) (CA INDEX NAME)



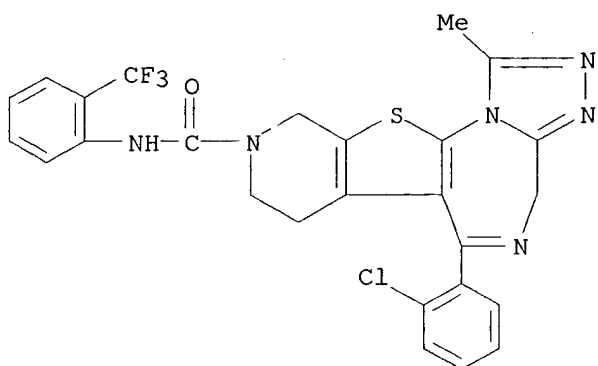
RN 252754-63-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[2-(trifluoromethyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



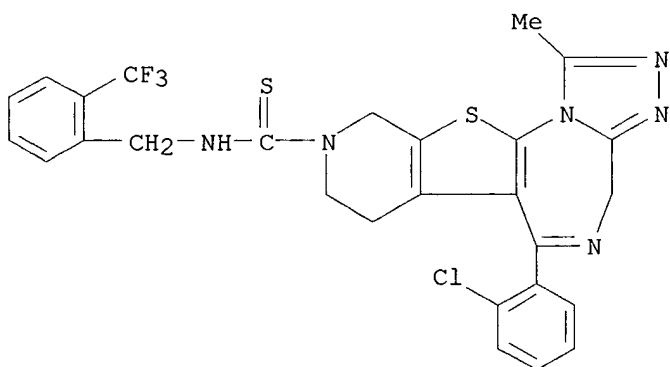
RN 252754-64-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 252754-65-7 CAPLUS

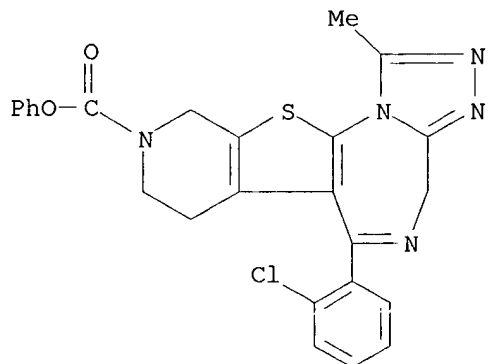
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[[2-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



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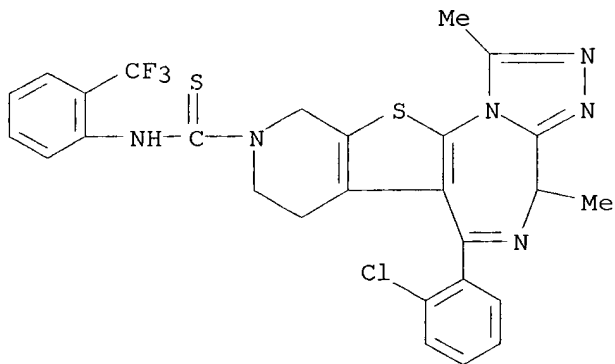
RN 252754-66-8 CAPLUS

4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, phenyl ester (9CI) (CA INDEX NAME)



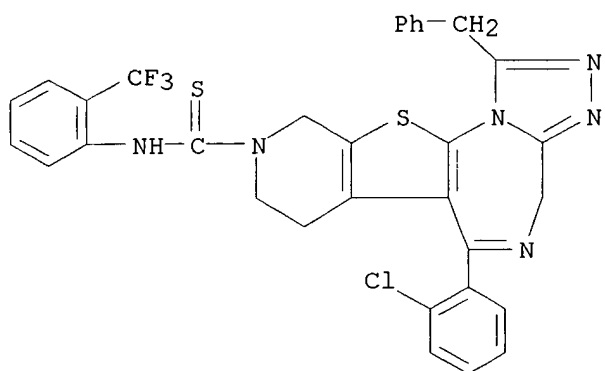
RN 252754-67-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



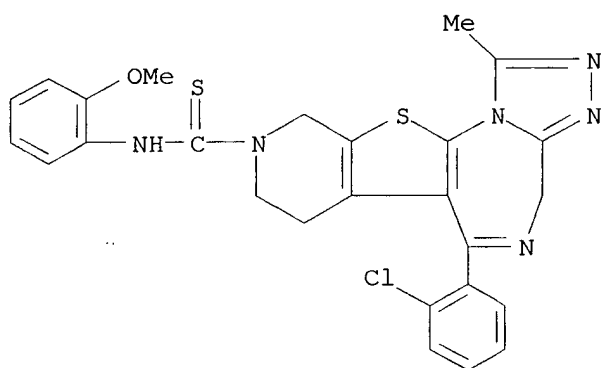
RN 252754-68-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-(phenylmethyl)-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



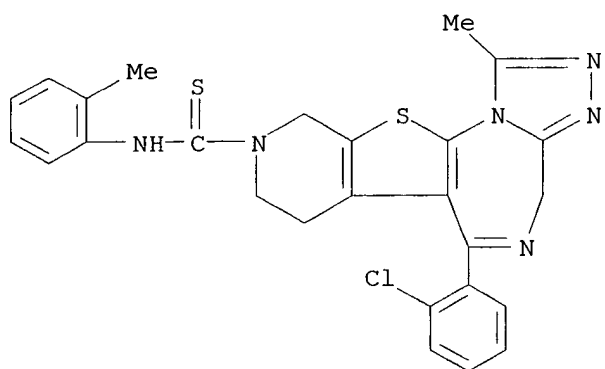
RN 252754-69-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(2-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-70-4 CAPLUS

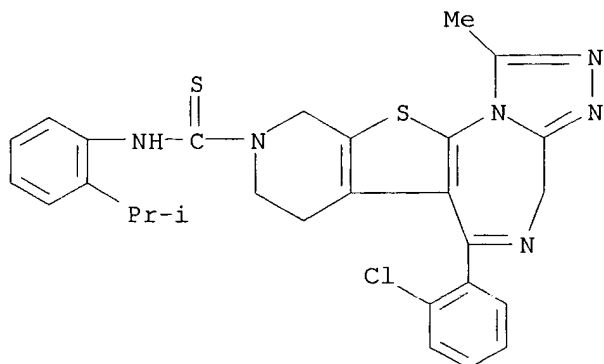
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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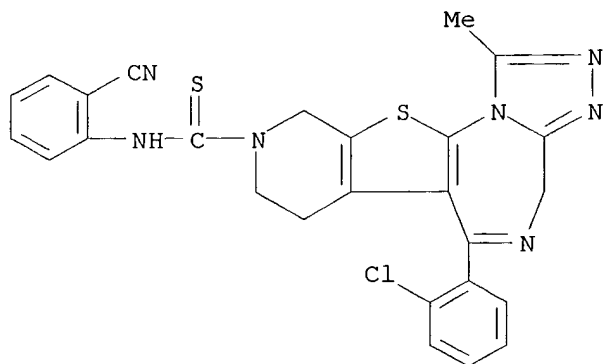
RN 252754-71-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(1-methylethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 252754-72-6 CAPLUS

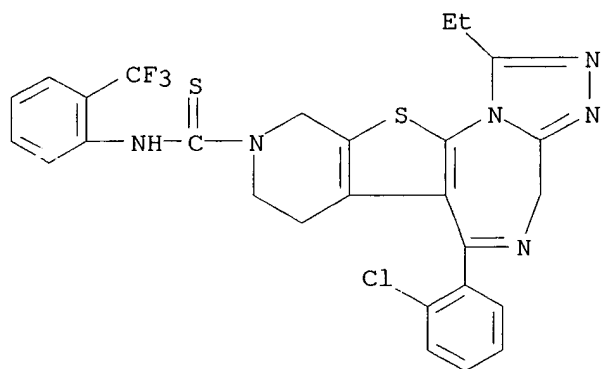
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-cyanophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-73-7 CAPLUS

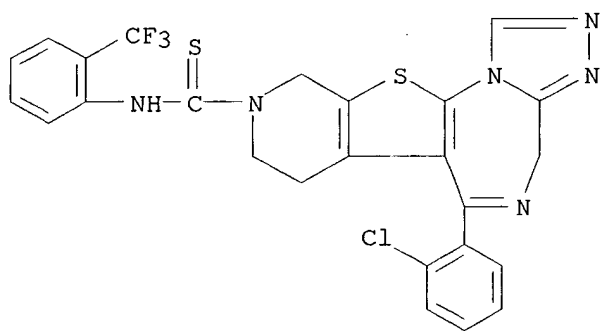
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-1-ethyl-7,10-dihydro-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

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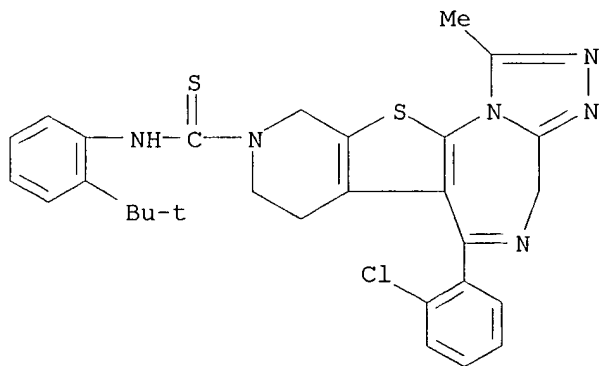
RN 252754-74-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



* RN 252754-75-9 CAPLUS

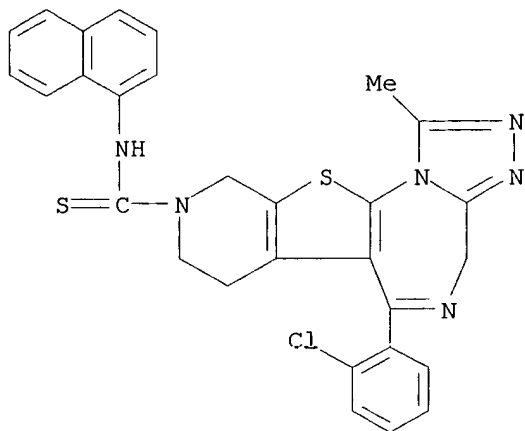
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-[2-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-76-0 CAPLUS

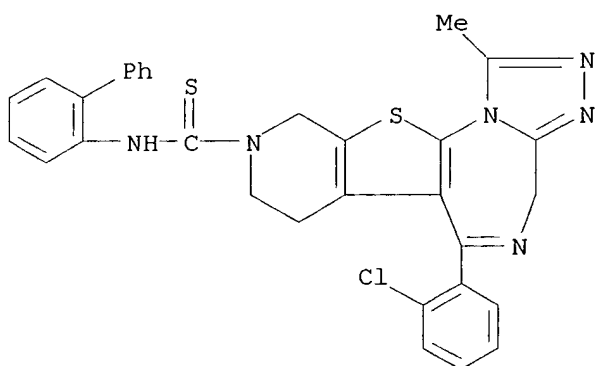
09/701,893

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-1-naphthalenyl- (9CI) (CA INDEX NAME)



RN 252754-77-1 CAPLUS

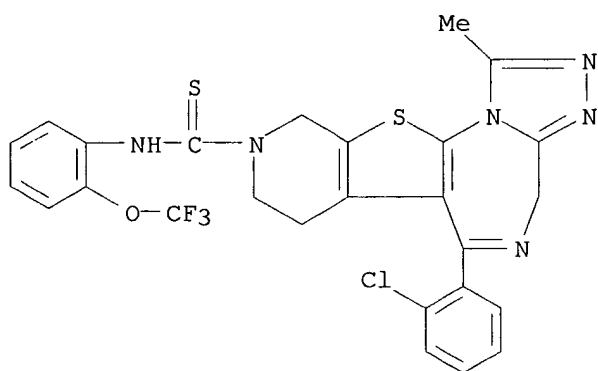
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[1,1'-biphenyl]-2-yl-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-78-2 CAPLUS

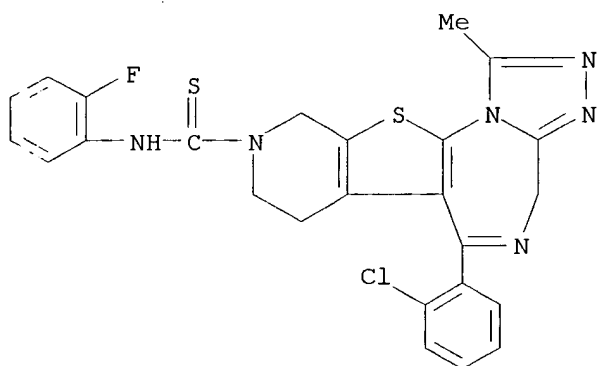
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)

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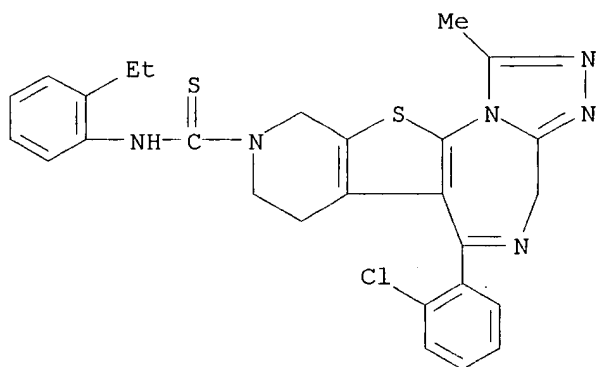
RN 252754-79-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-fluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-80-6 CAPLUS

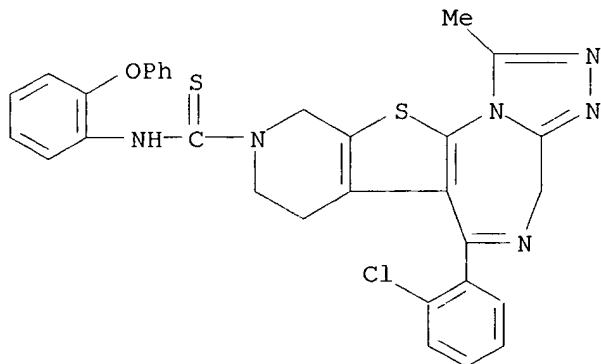
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-ethylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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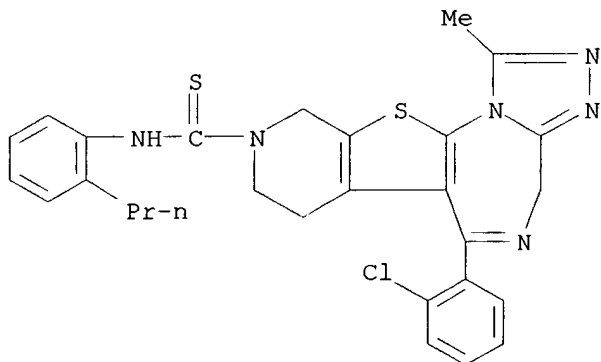
RN 252754-81-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 252754-82-8 CAPLUS

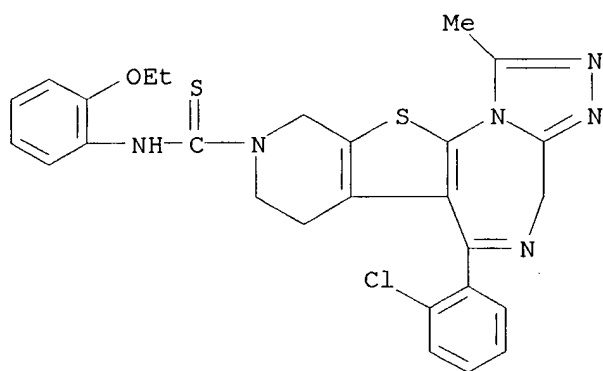
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-propylphenyl)- (9CI) (CA INDEX NAME)



RN 252754-83-9 CAPLUS

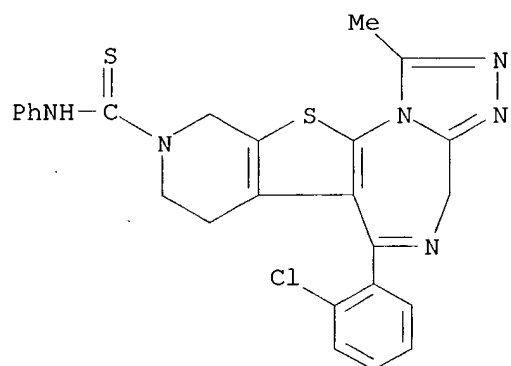
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-ethoxyphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

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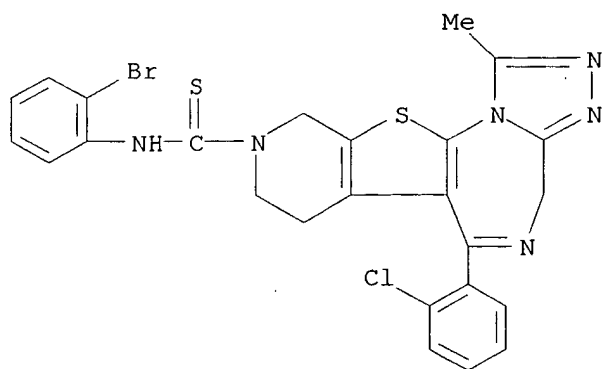
RN 252754-84-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-phenyl- (9CI) (CA INDEX NAME)



RN 252754-85-1 CAPLUS

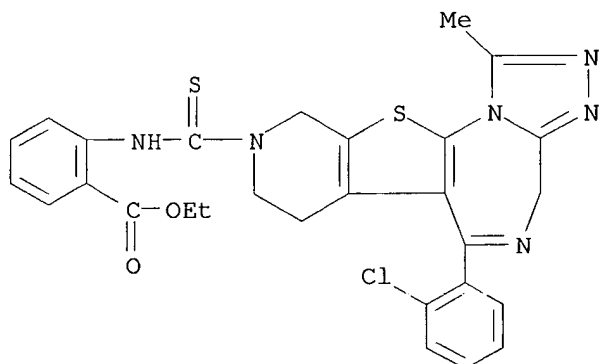
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(2-bromophenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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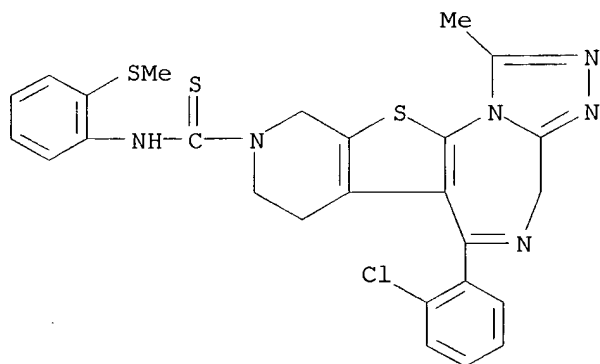
RN 252754-86-2 CAPLUS

CN Benzoic acid, 2-[[[6-(2-chlorophenyl)-7,10-dihydro-1-methyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]thioxomethyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



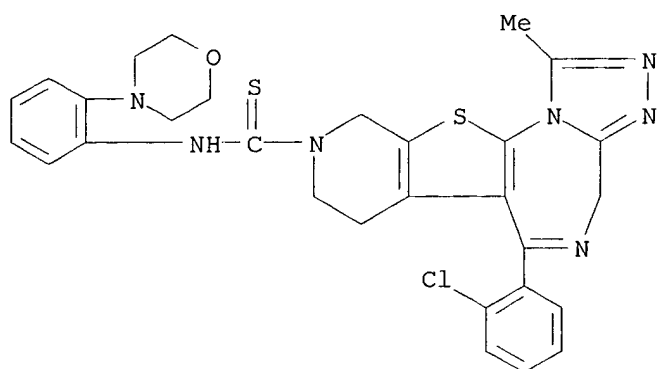
RN 252754-87-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)

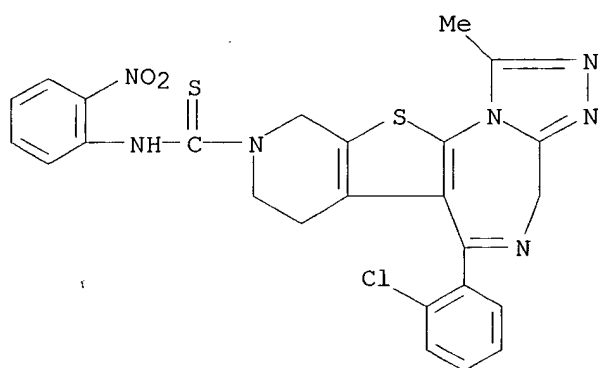


RN 252754-88-4 CAPLUS

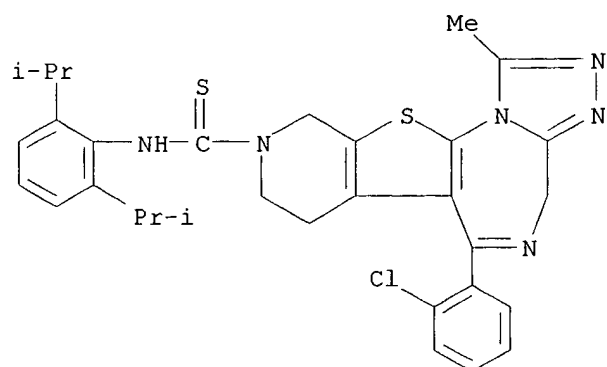
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 252754-89-5 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-nitrophenyl)- (9CI) (CA INDEX NAME)



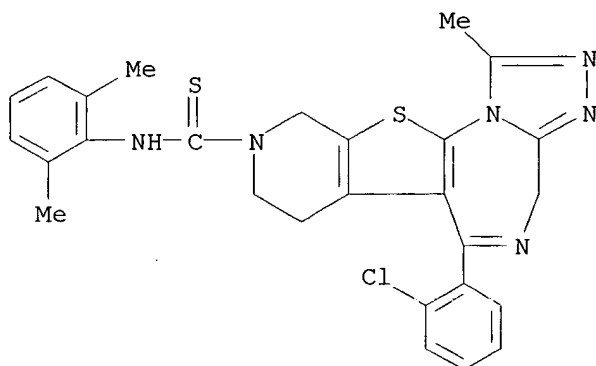
RN 252754-90-8 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[2,6-bis(1-methylethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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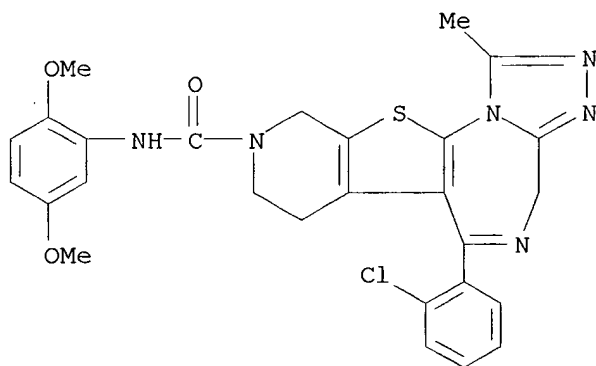
RN 252754-91-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,6-dimethylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



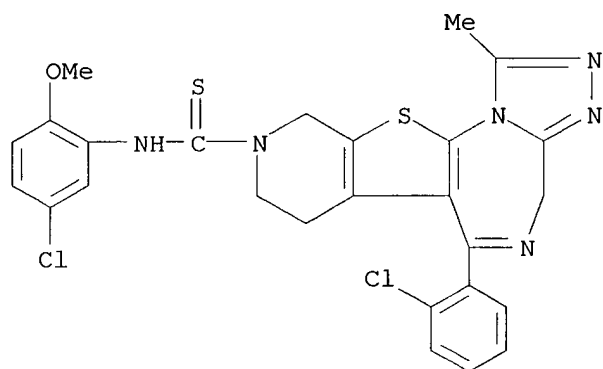
RN 252754-92-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,5-dimethoxyphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



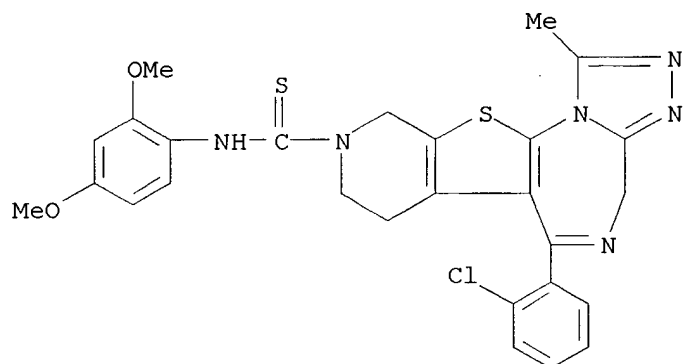
RN 252754-93-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(5-chloro-2-methoxyphenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



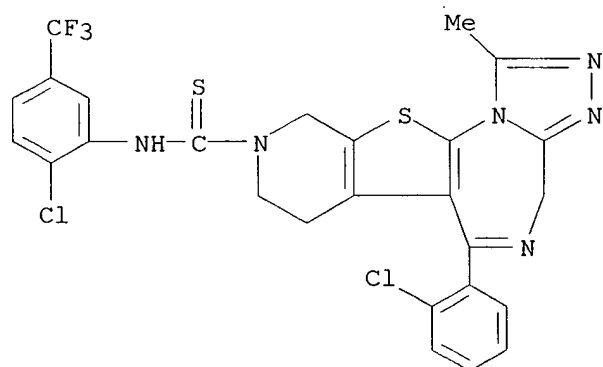
RN 252754-94-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,4-dimethoxyphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252754-95-3 CAPLUS

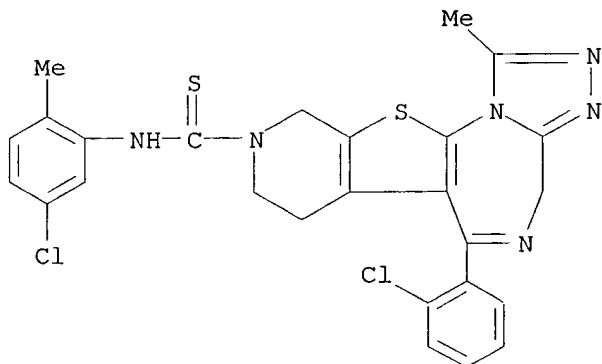
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-[2-chloro-5-(trifluoromethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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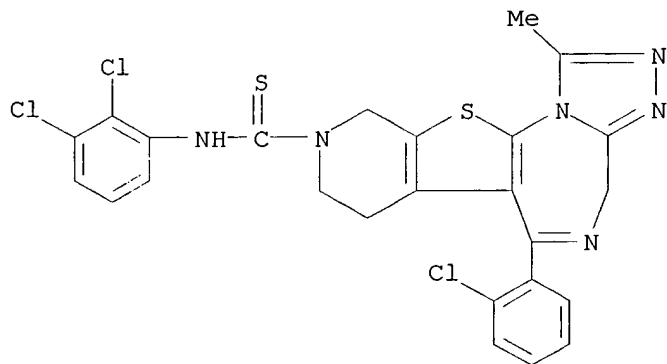
RN 252754-96-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(5-chloro-2-methylphenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



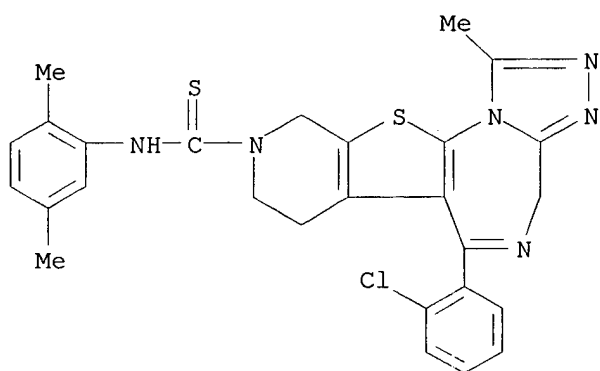
RN 252754-97-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,3-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



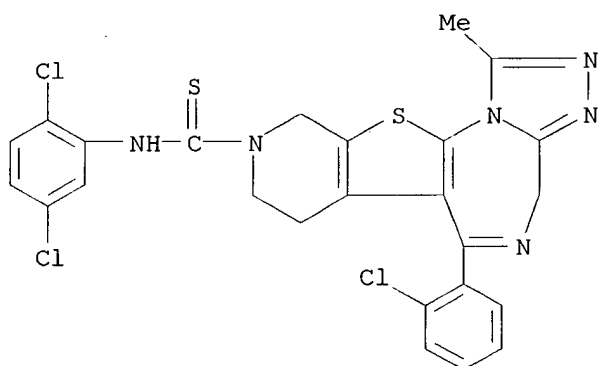
RN 252754-98-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,5-dimethylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



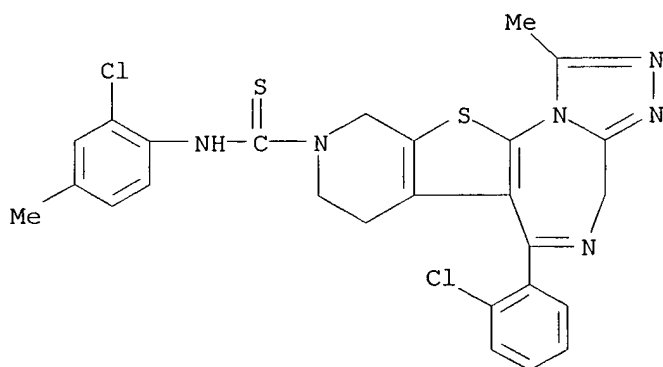
RN 252754-99-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,5-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-00-3 CAPLUS

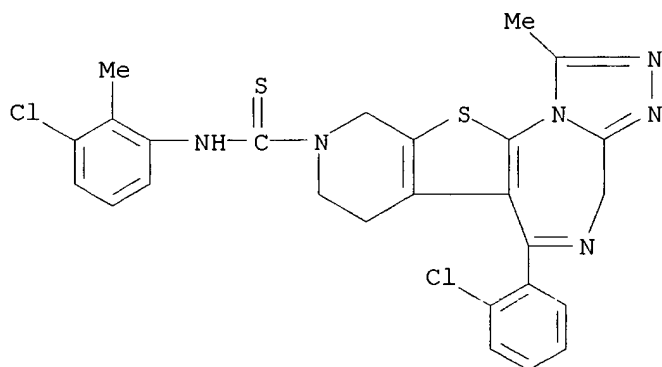
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(2-chloro-4-methylphenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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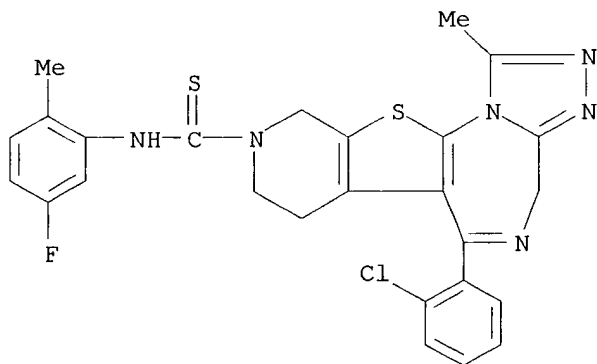
RN 252755-01-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(3-chloro-2-methylphenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-02-5 CAPLUS

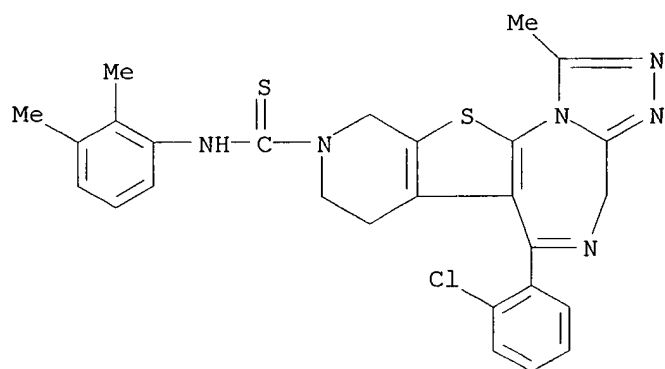
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(5-fluoro-2-methylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-03-6 CAPLUS

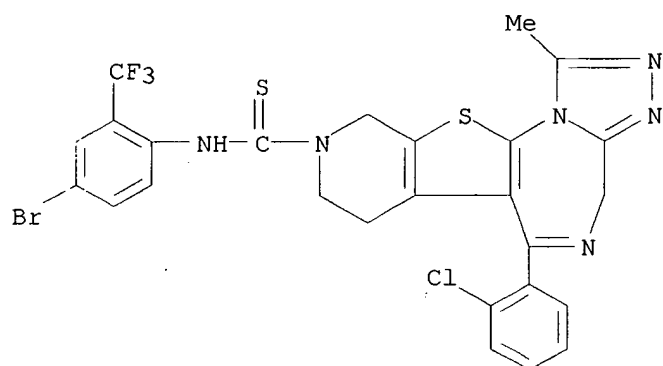
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,3-dimethylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

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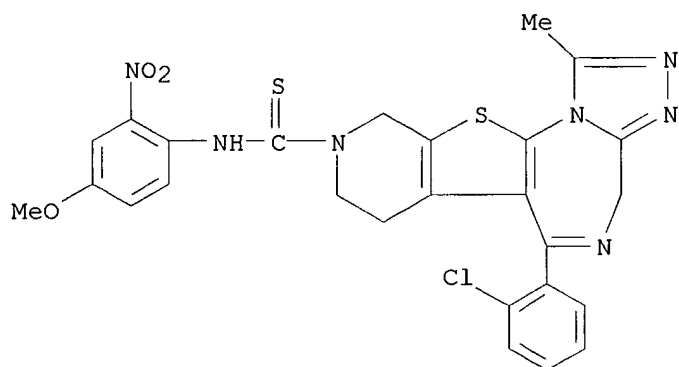
RN 252755-04-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[4-bromo-2-(trifluoromethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-05-8 CAPLUS

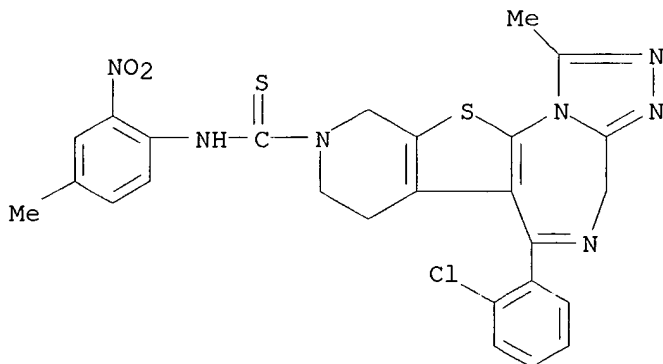
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



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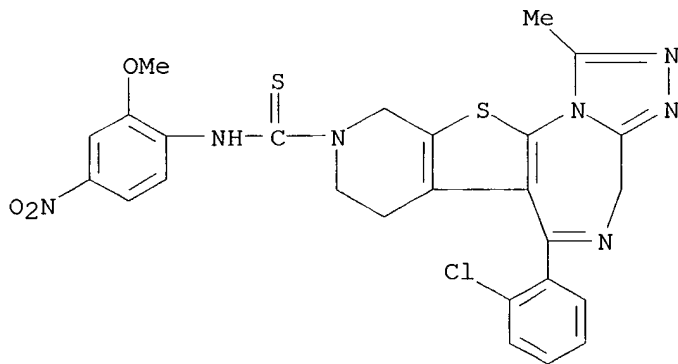
RN 252755-06-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-methyl-2-nitrophenyl)- (9CI) (CA INDEX NAME)



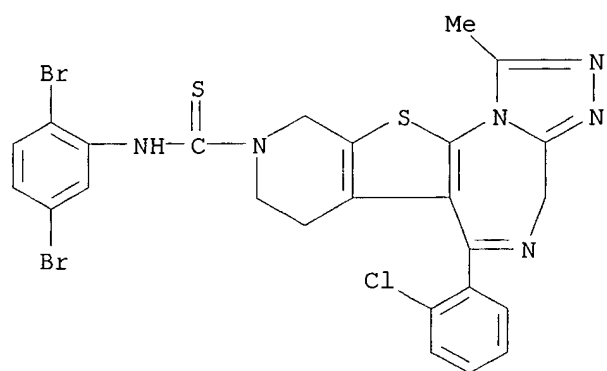
RN 252755-07-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(2-methoxy-4-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



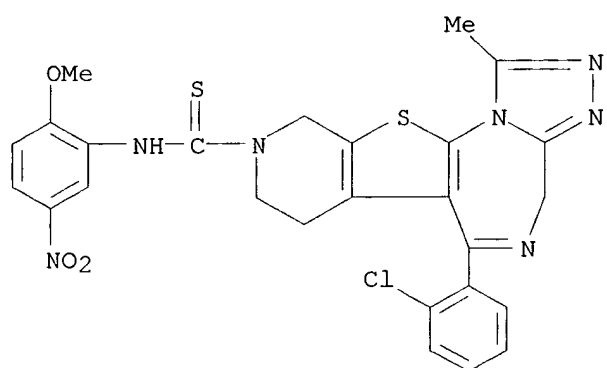
RN 252755-08-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2,5-dibromophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



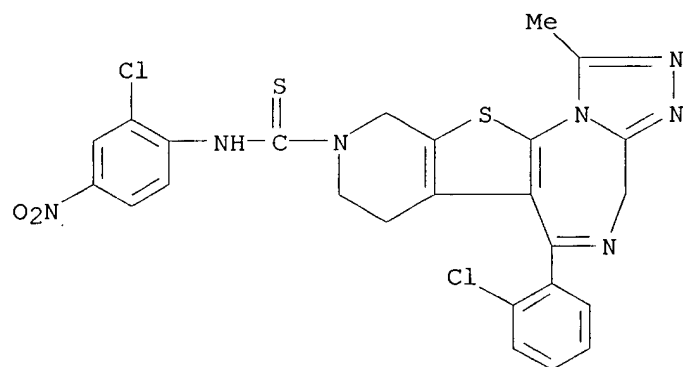
RN 252755-09-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(2-methoxy-5-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-10-5 CAPLUS

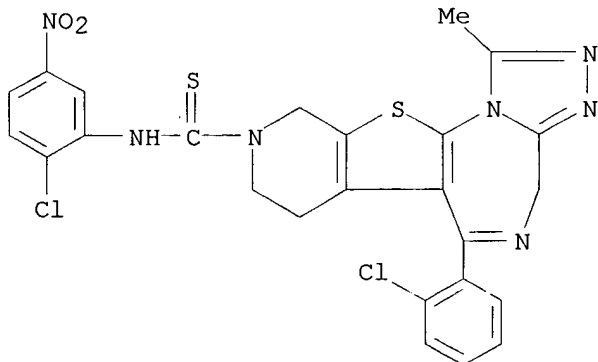
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(2-chloro-4-nitrophenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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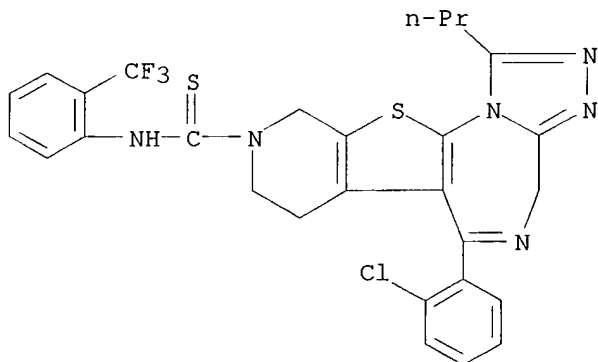
RN 252755-11-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(2-chloro-5-nitrophenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



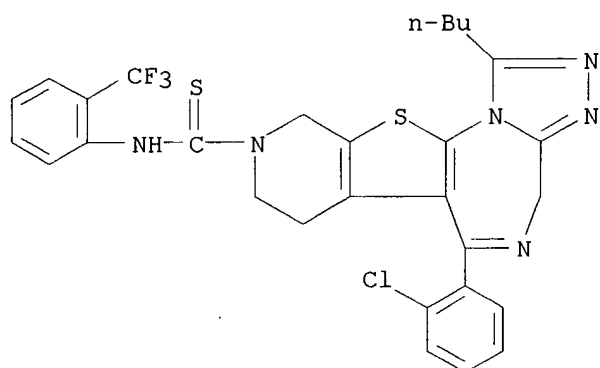
RN 252755-13-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-propyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



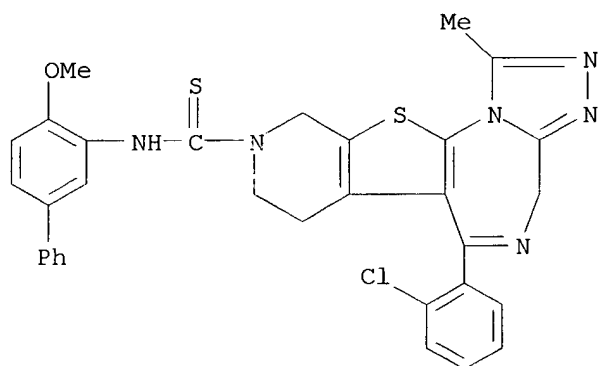
RN 252755-15-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 1-butyl-6-(2-chlorophenyl)-7,10-dihydro-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



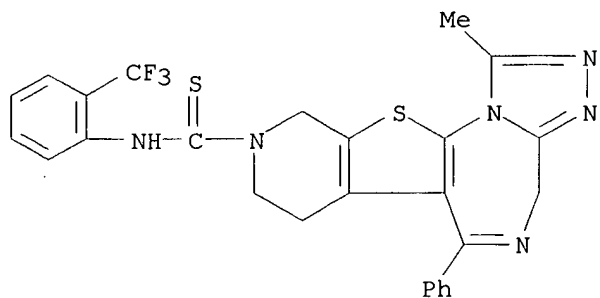
RN 252755-16-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy[1,1'-biphenyl]-3-yl)-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-17-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 7,10-dihydro-1-methyl-6-phenyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

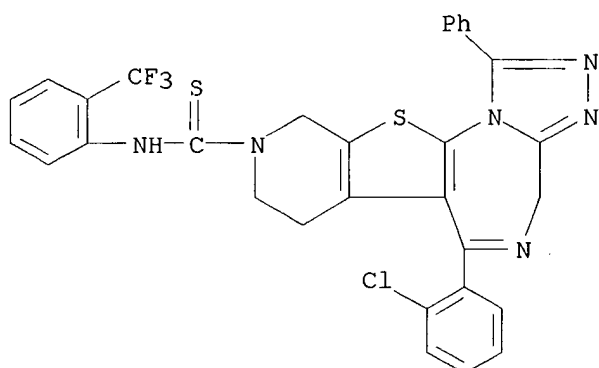


RN 252755-18-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-phenyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

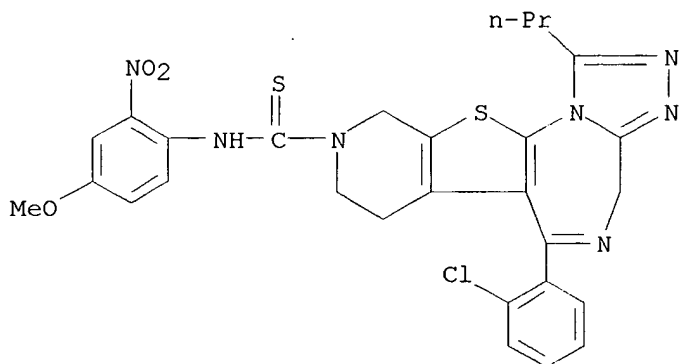
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(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 252755-20-7 CAPLUS

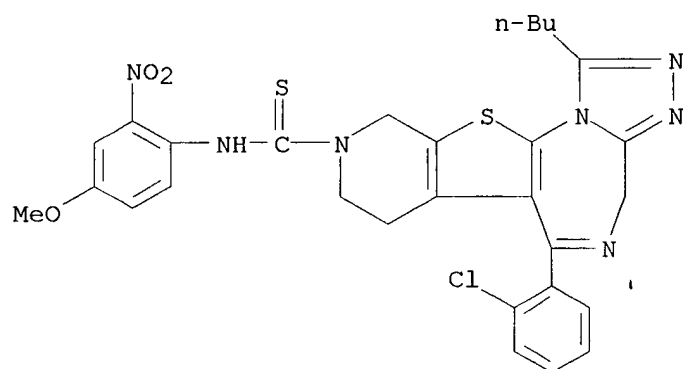
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-propyl- (9CI) (CA INDEX NAME)



RN 252755-21-8 CAPLUS

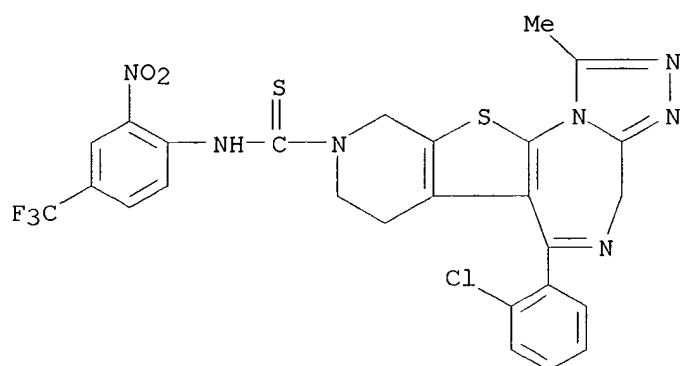
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 1-butyl-6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-2-nitrophenyl)- (9CI) (CA INDEX NAME)

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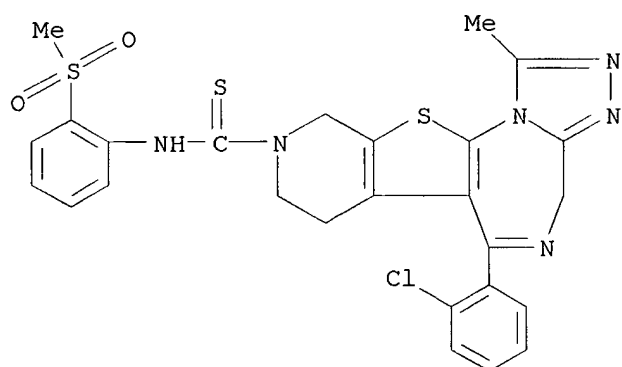
PN 252755-22-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-nitro-4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 252755-23-0 CAPLUS

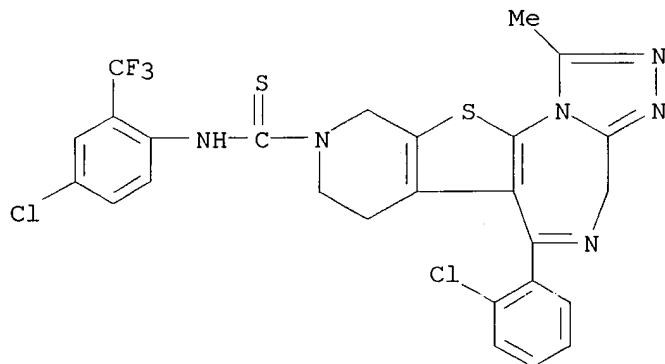
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



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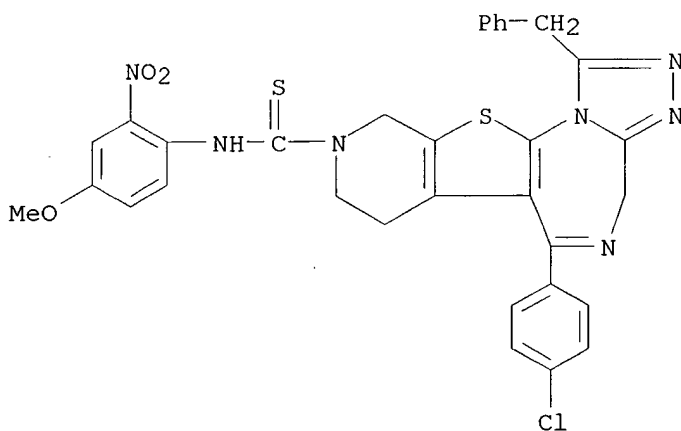
RN 252755-24-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-[4-chloro-2-(trifluoromethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-25-2 CAPLUS

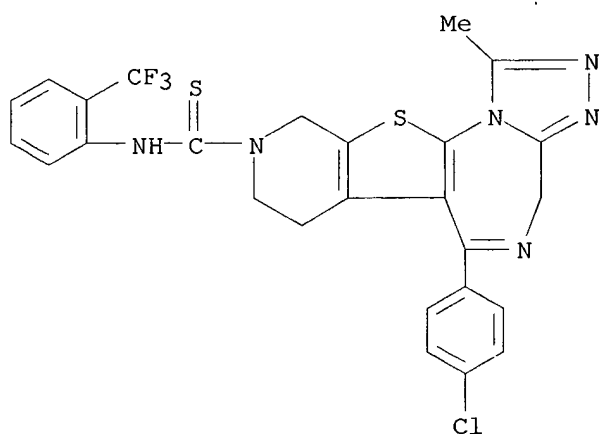
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 252755-26-3 CAPLUS

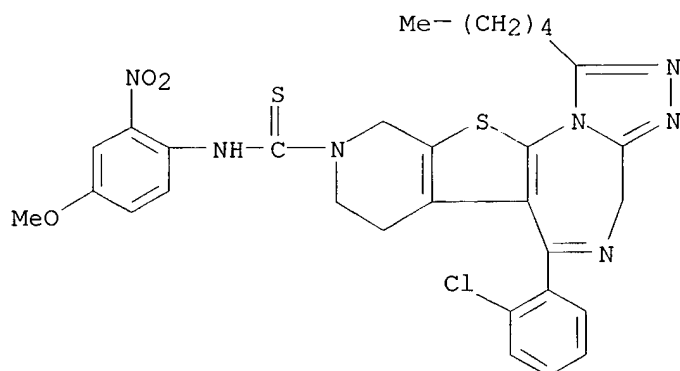
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

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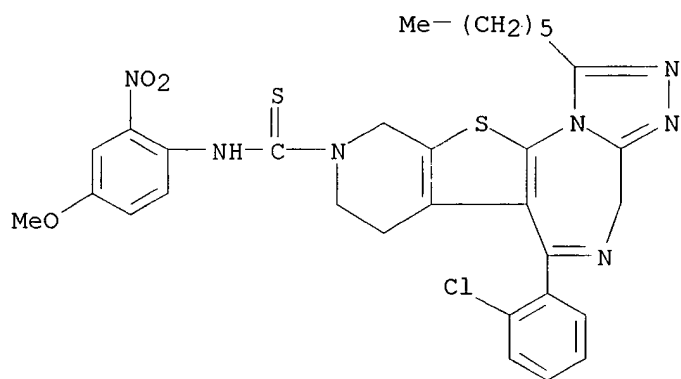
RN 252755-27-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-pentyl- (9CI) (CA INDEX NAME)



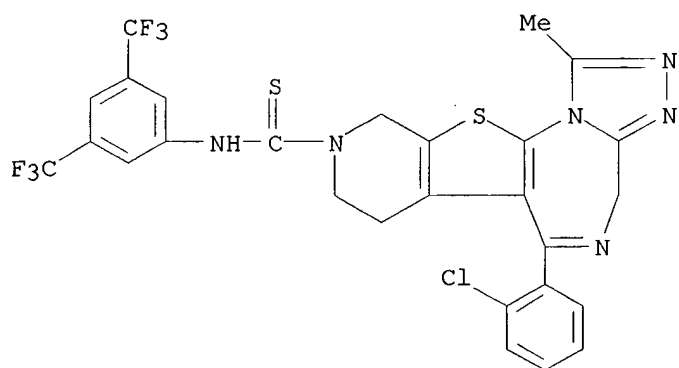
RN 252755-28-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-1-hexyl-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)



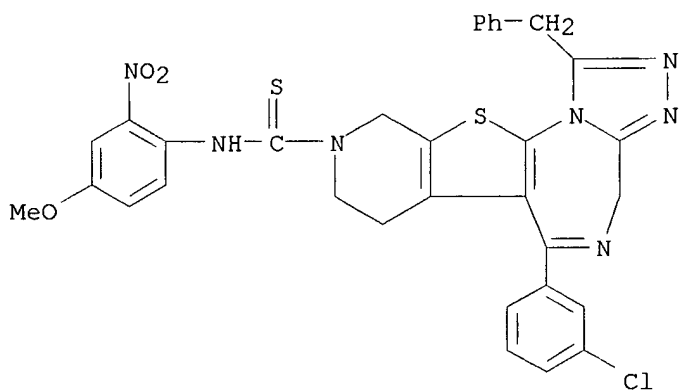
RN 252755-29-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[3,5-bis(trifluoromethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



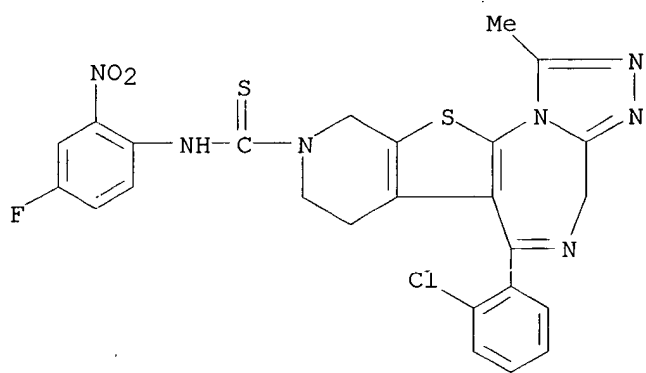
RN 252755-30-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(3-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



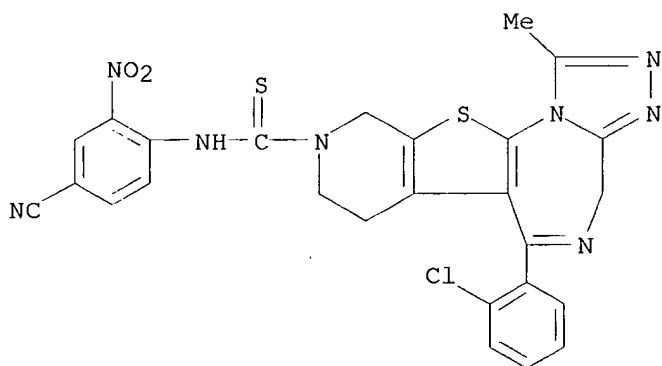
RN 252755-31-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-fluoro-2-nitrophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



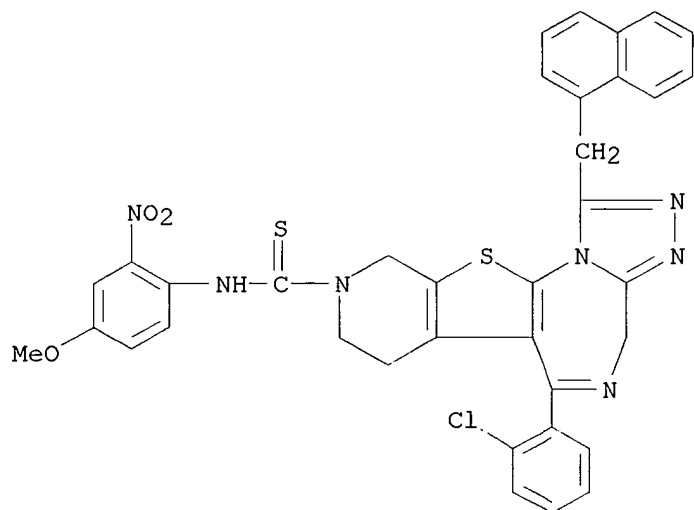
RN 252755-32-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-cyano-2-nitrophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



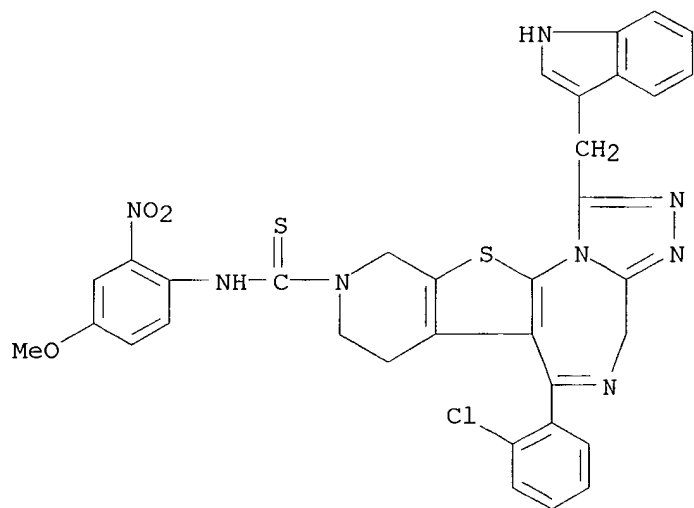
RN 252755-33-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-(1-naphthalenylmethyl)- (9CI) (CA INDEX NAME)



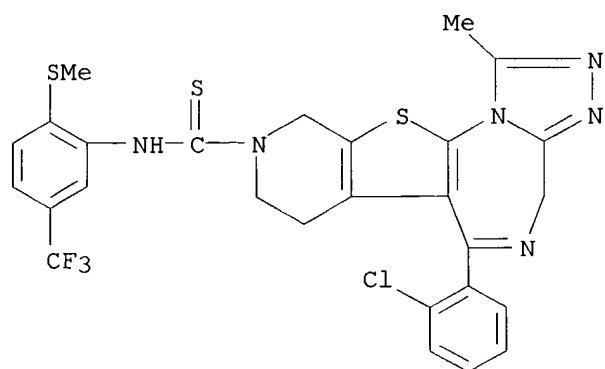
RN 252755-34-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-(1H-indol-3-ylmethyl)-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)



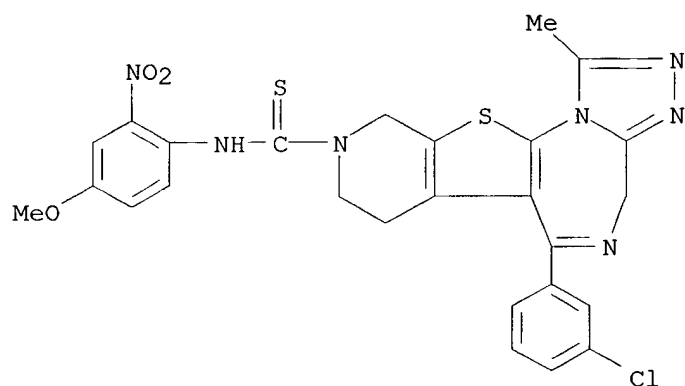
RN 252755-35-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(methylthio)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



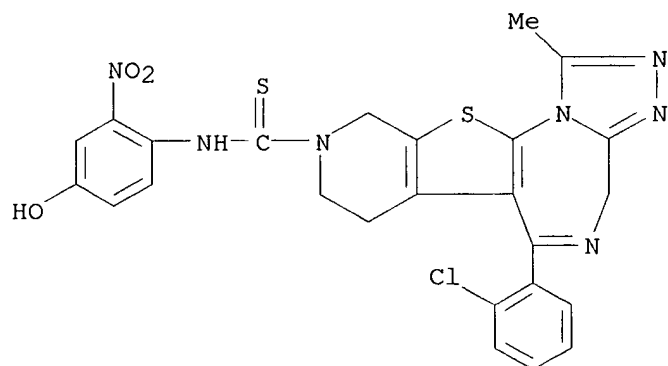
RN 252755-36-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(3-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



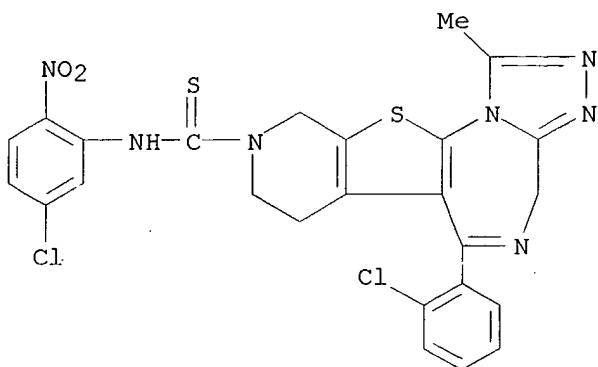
RN 252755-38-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-hydroxy-2-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



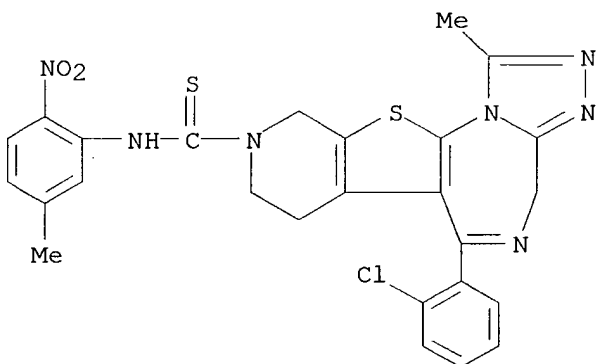
RN 252755-39-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(5-chloro-2-nitrophenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-40-1 CAPLUS

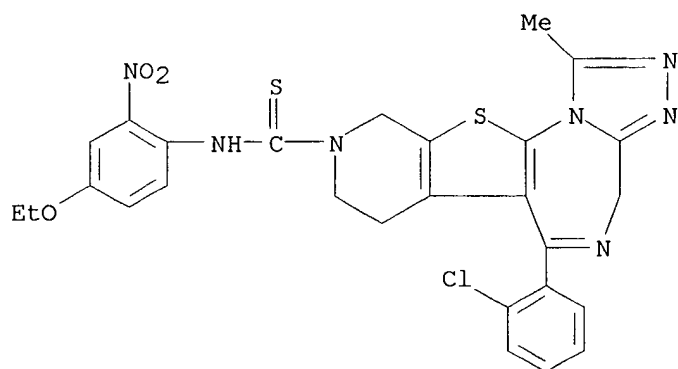
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(5-methyl-2-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 252755-41-2 CAPLUS

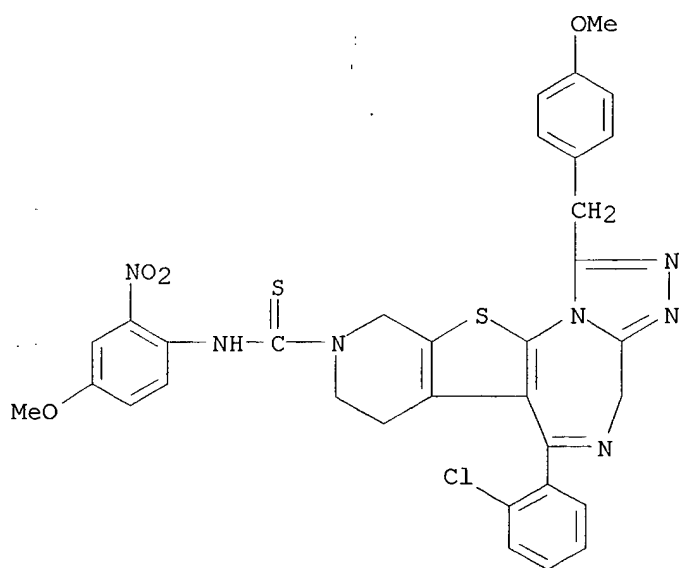
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-ethoxy-2-nitrophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

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RN 252755-42-3 CAPLUS

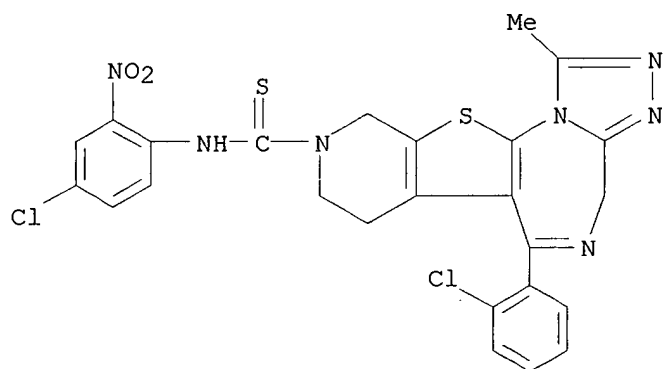
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 252755-43-4 CAPLUS

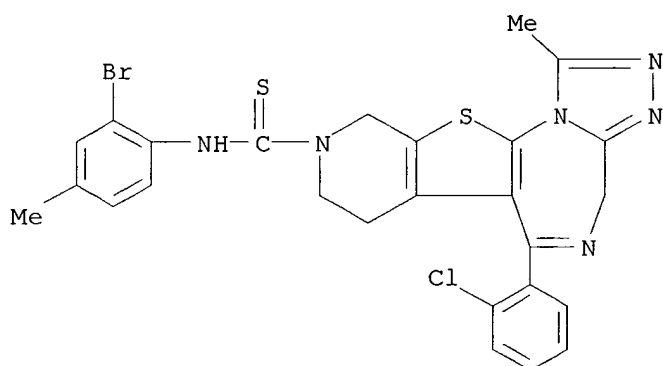
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(4-chloro-2-nitrophenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

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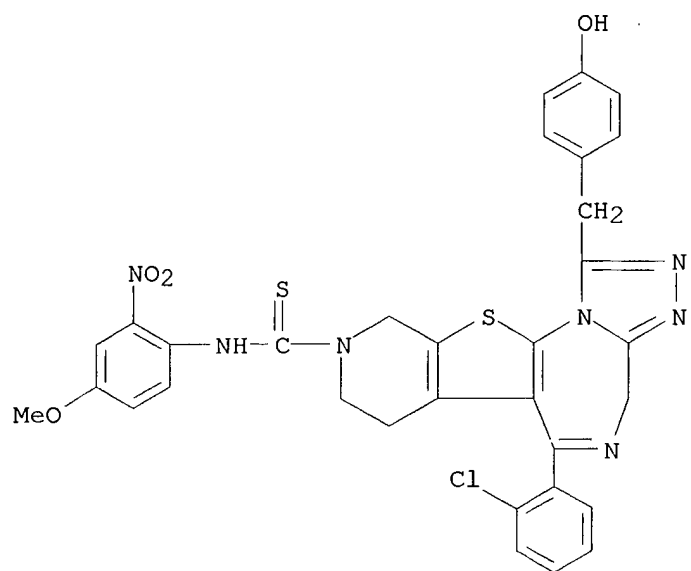
RN 252755-44-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-(2-bromo-4-methylphenyl)-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



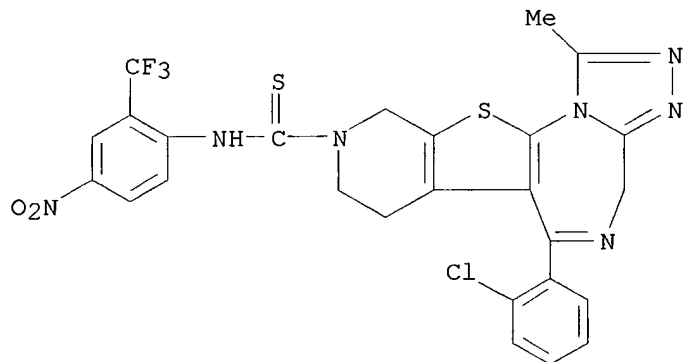
RN 252755-45-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-[(4-hydroxyphenyl)methyl]-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)



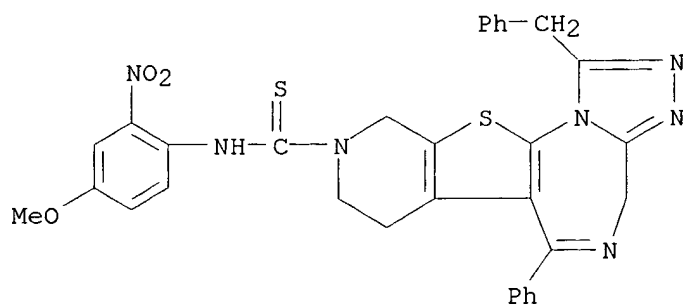
RN 252755-46-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-nitro-2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



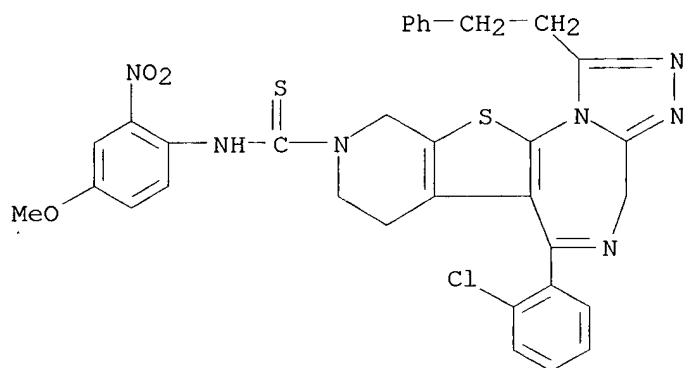
RN 252755-47-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-6-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



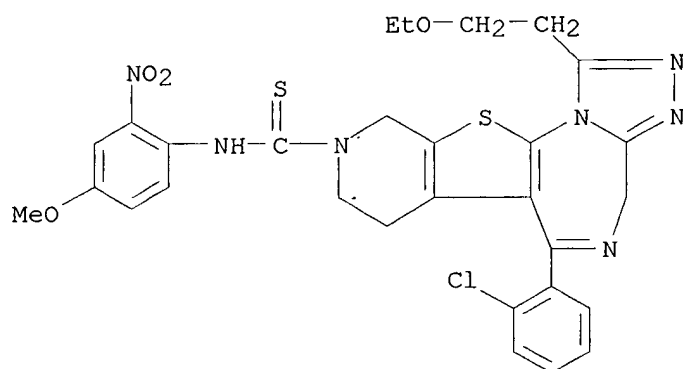
RN 252755-49-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 252755-50-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-1-(2-ethoxyethyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)

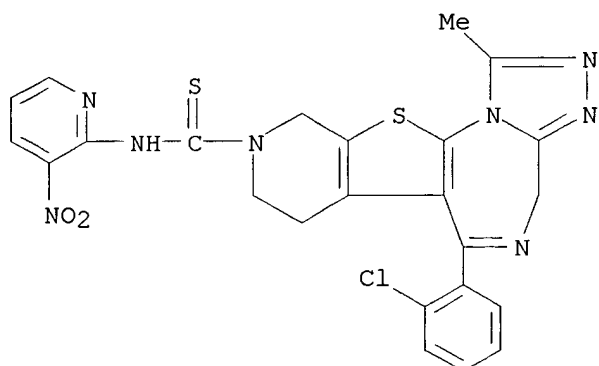


RN 252755-51-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3-nitro-4-methoxyphenyl)- (9CI) (CA INDEX NAME)

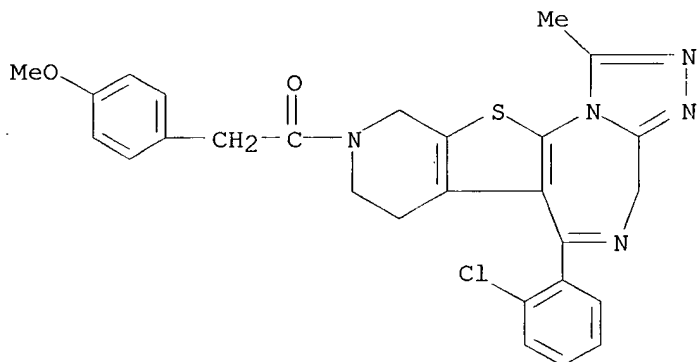
09/701,893

2-pyridinyl)- (9CI) (CA INDEX NAME)



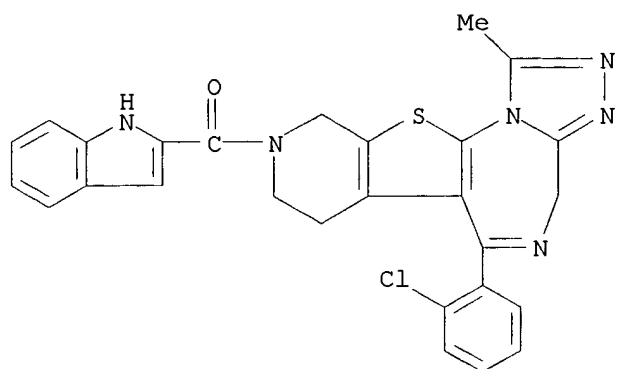
RN 252755-52-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(4-methoxyphenyl)acetyl]-1-
methyl- (9CI) (CA INDEX NAME)



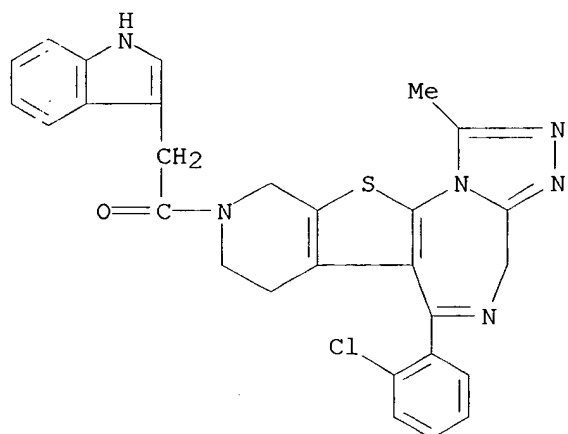
RN 252755-53-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-(1H-indol-2-ylcarbonyl)-1-methyl-
(9CI) (CA INDEX NAME)



RN 252755-54-7 CAPLUS

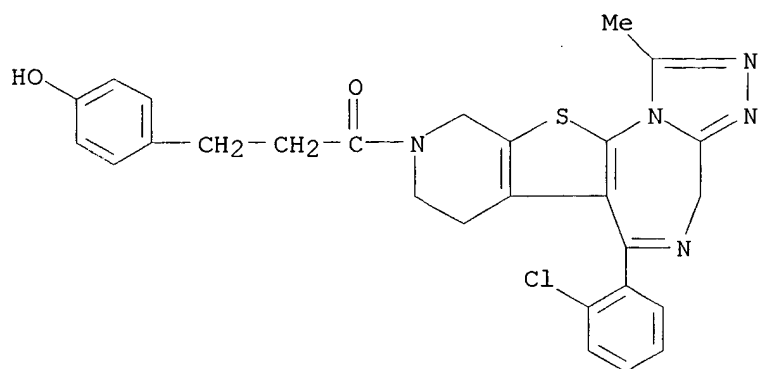
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-(1H-indol-3-ylacetyl)-1-methyl-
(9CI) (CA INDEX NAME)



RN 252755-55-8 CAPLUS

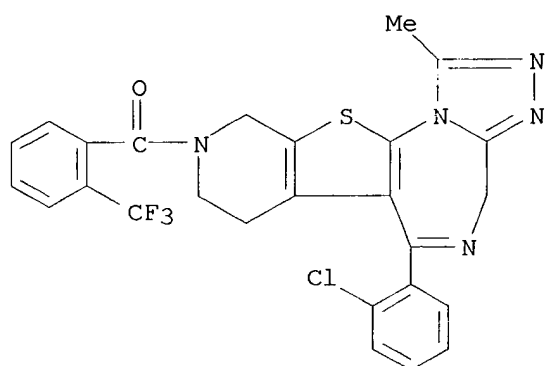
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[3-(4-hydroxyphenyl)-1-oxopropyl]-
1-methyl- (9CI) (CA INDEX NAME)

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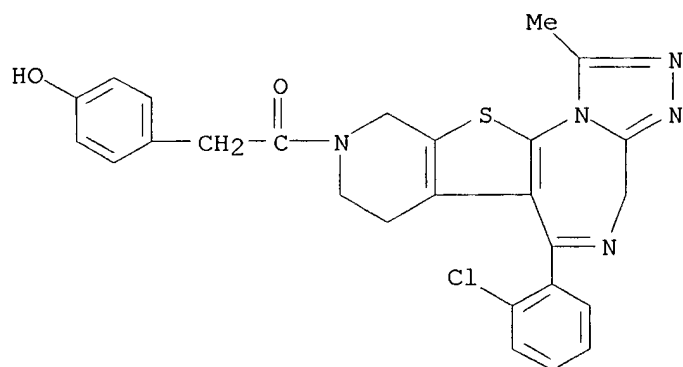
RN 252755-56-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)



RN 252755-57-0 CAPLUS

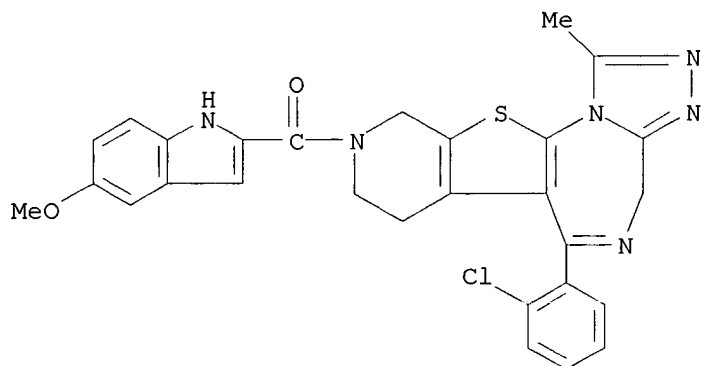
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(4-hydroxyphenyl)acetyl]-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

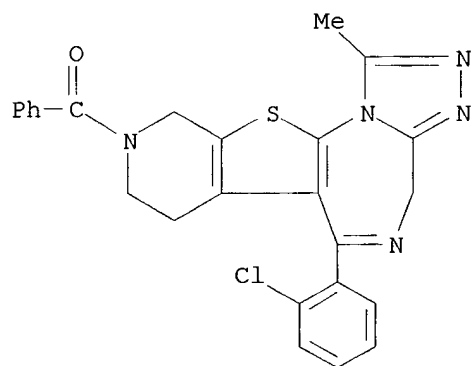
RN 252755-59-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(5-methoxy-1H-indol-2-
yl)carbonyl]-1-methyl- (9CI) (CA INDEX NAME)



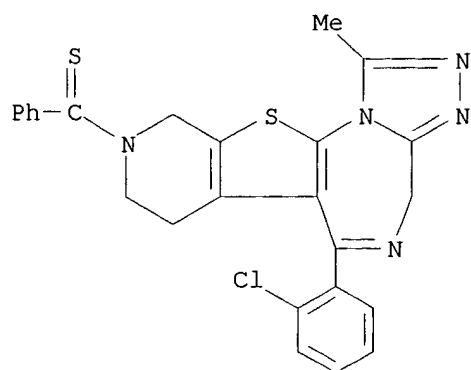
RN 252755-60-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-benzoyl-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA
INDEX NAME)



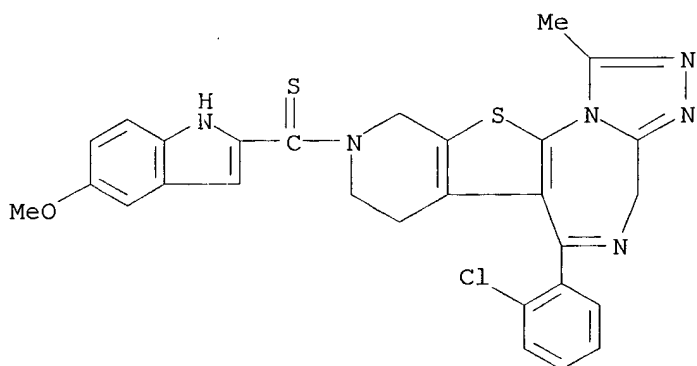
RN 252755-61-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(phenylthioxomethyl)-
(9CI) (CA INDEX NAME)



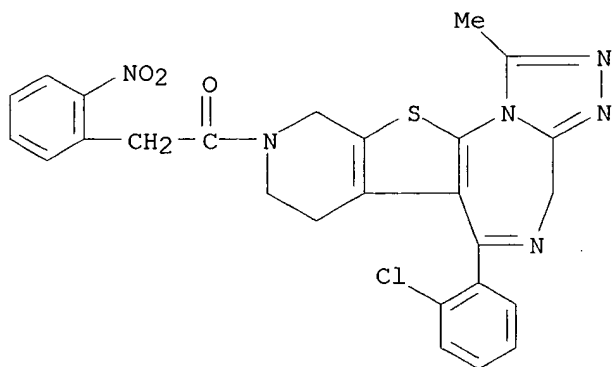
RN 252755-62-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(5-methoxy-1H-indol-2-yl)thioxomethyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 252755-63-8 CAPLUS

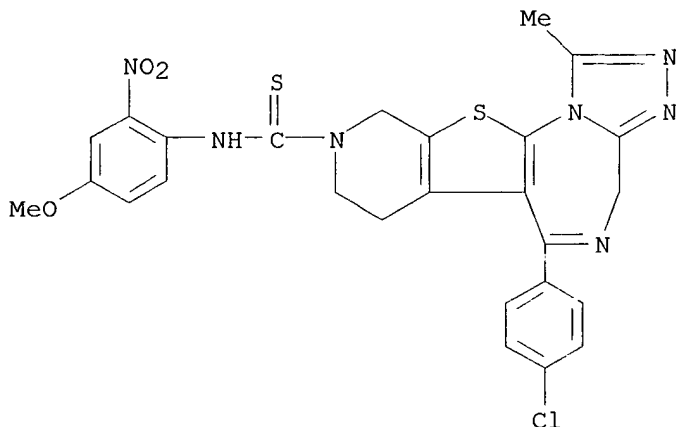
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-nitrophenyl)acetyl]-
(9CI) (CA INDEX NAME)



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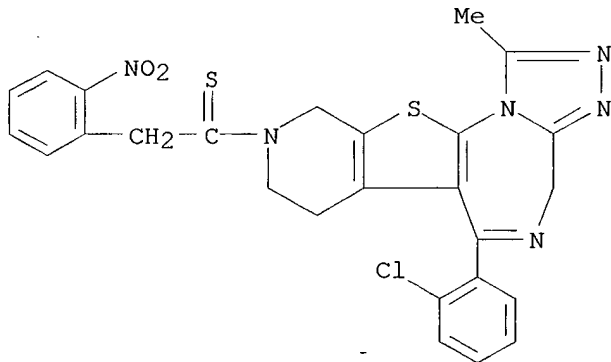
RN 252755-64-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-methyl- (9CI) (CA INDEX NAME)



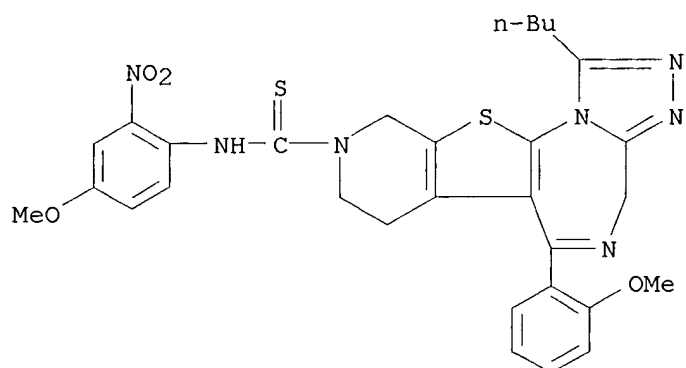
RN 252755-65-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-nitrophenyl)-1-thioxoethyl]- (9CI) (CA INDEX NAME)



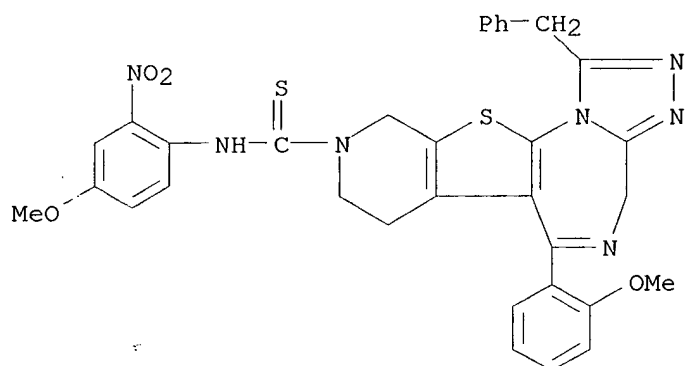
RN 252755-67-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 1-butyl-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



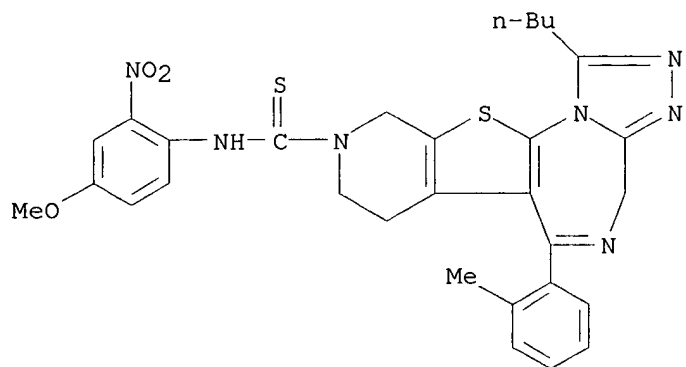
RN 252755-68-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-6-(2-methoxyphenyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 252755-69-4 CAPLUS

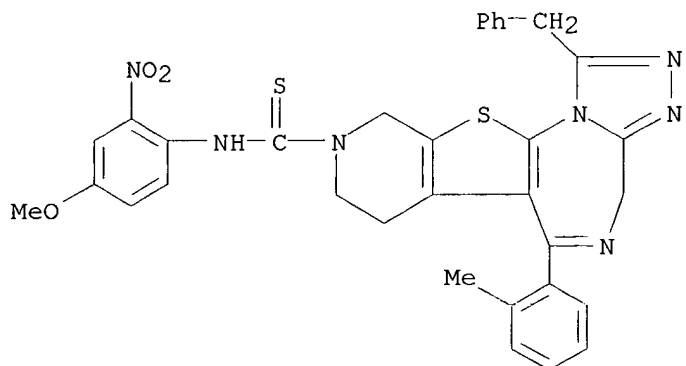
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 1-butyl-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-6-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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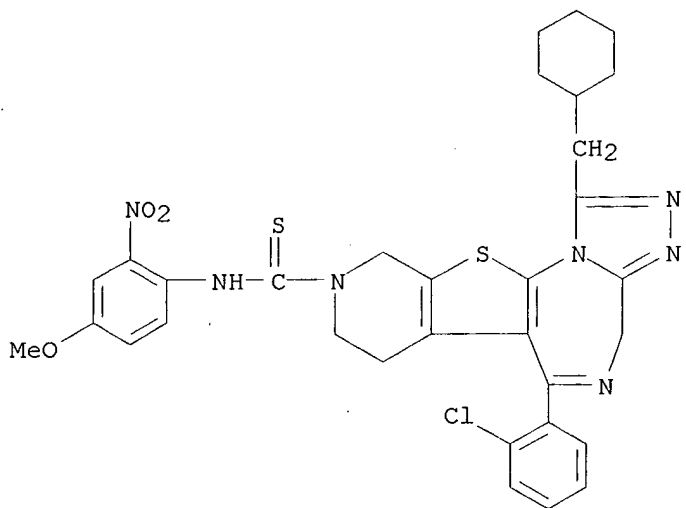
RN 252755-70-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-6-(2-methylphenyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



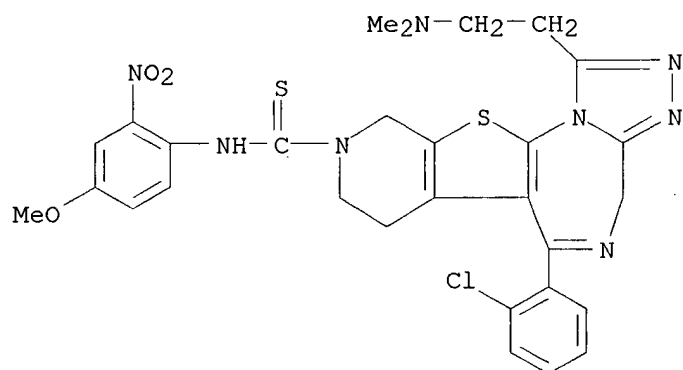
RN 252755-71-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-1-(cyclohexylmethyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)

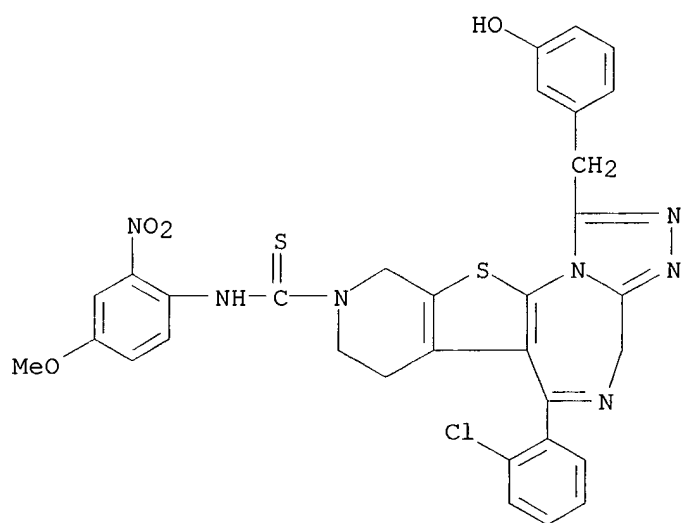


RN 252755-72-9 CAPLUS

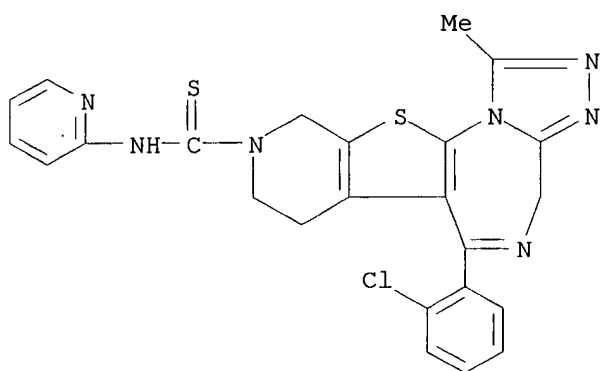
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-1-[2-(dimethylamino)ethyl]-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 252755-74-1 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
 9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-[(3-
 hydroxyphenyl)methyl]-N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)

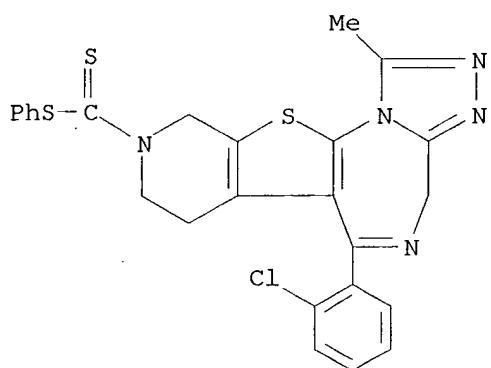


RN 252755-75-2 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
 9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-2-
 pyridinyl- (9CI) (CA INDEX NAME)



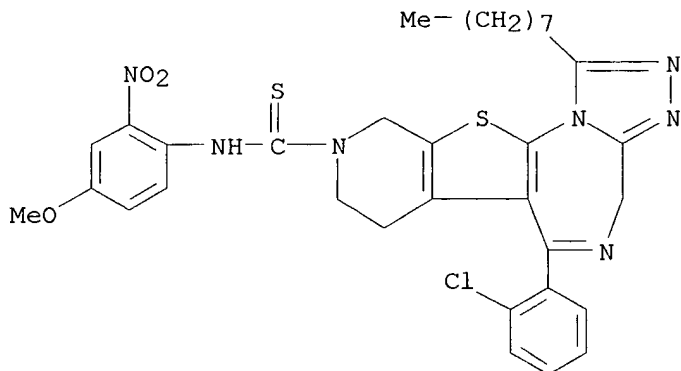
RN 252755-76-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbodithioic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, phenyl ester (9CI) (CA INDEX NAME)



RN 252755-80-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxy-2-nitrophenyl)-1-octyl- (9CI) (CA INDEX NAME)



09/701,893

RN 252879-75-7 CAPLUS

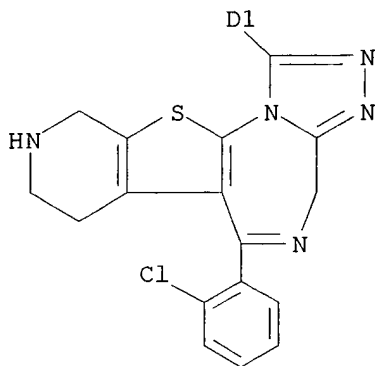
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
1-[1,1'-biphenyl]yl-6-(2-chlorophenyl)-7,8,9,10-tetrahydro- (9CI) (CA
INDEX NAME)

PAGE 1-A



D1- Ph

PAGE 2-A



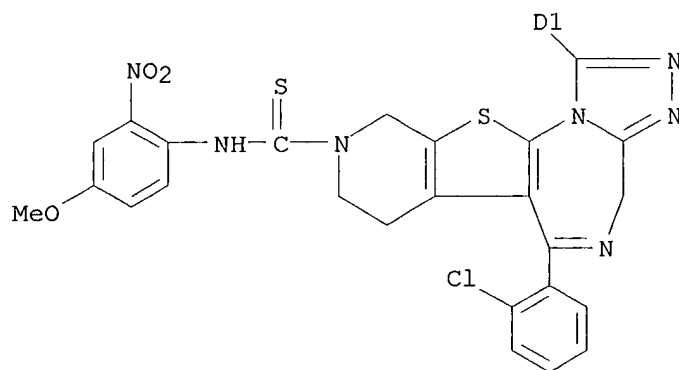
RN 252879-76-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 1-[1,1'-biphenyl]yl-6-(2-chlorophenyl)-7,10-dihydro-
N-(4-methoxy-2-nitrophenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



D1- Ph



RE.CNT 3

RE

- (1) Doly, M; Ophthalmic Research 1993, V25, P314 CAPLUS
- (2) Rabinovici, R; Journal of Pharmacology and Experimental Therapeutics 1990, V255(1), P256 CAPLUS
- (3) Yoshitomi; EP 0638560 A 1995 CAPLUS

09/701,893

L23 ~~ANSWER 9 OF 92~~ CAPLUS COPYRIGHT 2001 ACS

AN 1999:714474 CAPLUS

DN 132:49675

TI Determination of the kinetic constants of the reversible opening of a triazolo-1,4-thienodiazepine in water at different pH values: a striking example of the determination of intimately intricate kinetic and equilibrium constants

AU Legouin, B.; Burgot, J.-L.

CS Laboratoire de Chimie Analytique et Bromatologie, U.F.R. des Sciences Pharmaceutiques et Biologiques, Rennes, 35043, Fr.

SO Int. J. Chem. Kinet. (1999), 31(11), 826-837
CODEN: IJCKBO; ISSN: 0538-8066

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB Apparent kinetic consts. of the reversible opening of a triazolo-1,4-thienodiazepine were detd. by UV-spectrophotometry and by polarog. in H₂O at several pH values assuming as a hypothesis a stationary state for the carbinolamine intermediate. Both the apparent kinetic consts., *k_f* and *k_r*, exhibited a max. for the values H₀ = -0.25 and pH = 6.07. A possible detn. of the elementary kinetic consts. of the several acido-basic species which may be involved in the opening and closing process according to the pH and p*K_a* values was studied and is discussed. The results are consistent with the hypothesis that both the opening of the diazepine cycle and the closing of the opened form proceed through a mechanism suggesting that the protonated form of the carbinolamine function of the intermediate is involved.

ET 114800-58-7 252979-77-4 252979-78-5

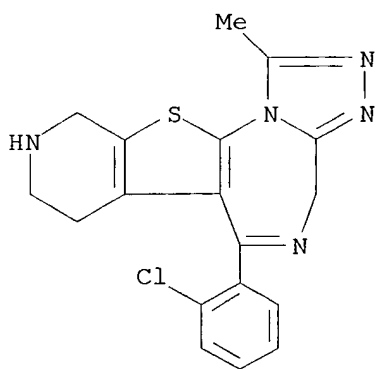
252979-79-6

RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process)

(acid-base equil.; kinetic and equil. consts. for pH dependence of reversible opening of aq. triazolo-1,4-thienodiazepine deriv.)

RN 114800-58-7 CAPLUS

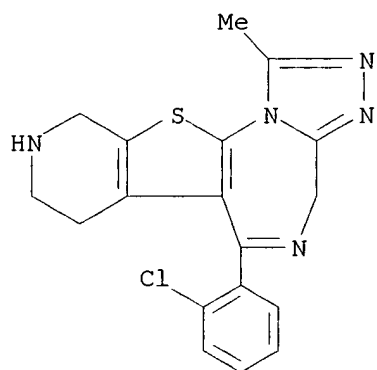
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 252979-77-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-, conjugate monoacid (9CI) (CA INDEX NAME)

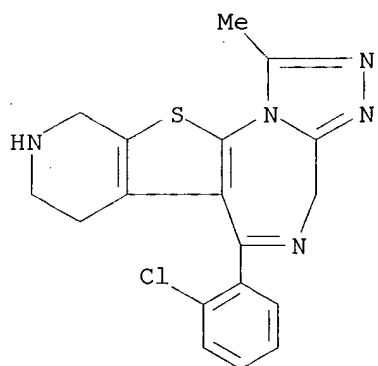
09/701,893



● H⁺

RN 252979-78-5 CAPLUS

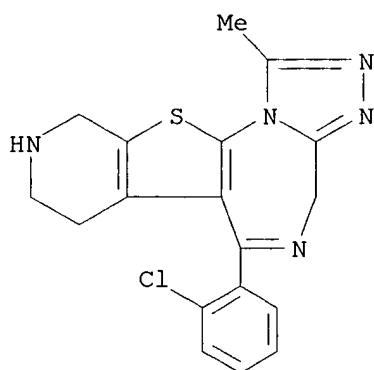
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-, conjugate diacid (9CI)
(CA INDEX NAME)



● 2 H⁺

RN 252979-79-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-, conjugate triacid (9CI)
(CA INDEX NAME)



● 3 H⁺

RE.CNT 18

RE

- (3) Edsall, J; Proc Natl Acad Sci 1958, V44, P505 CAPLUS
 - (4) Gallo, B; Anal Lett 1986, V19, P1853 CAPLUS
 - (5) Inotsume, N; Chem Pharm Bull 1980, V28, P2536 CAPLUS
 - (6) Jimenez, R; Fresenius Z Anal Chem 1987, V329, P468 CAPLUS
 - (7) Konishi, M; J Pharm Sci 1982, V71, P1328 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~LA~~3 ANSWER 10 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1999:494800 CAPLUS

~~DN~~ 131:165039

TI Effect of a platelet activating factor receptor antagonist on sensitivity to cis-diamminedichloroplatinum (II) in human pulmonary adenocarcinoma cell lines

AU Heki, Utako

CS Department of Internal Medicine (III), School of Medicine, Kanazawa University, Kanazawa, 920-8640, Japan

SO Kanazawa Daigaku Juzen Igakkai Zasshi (1999), 108(2), 224-232
CODEN: JUZIAG; ISSN: 0022-7226

PB Juzen Igakkai

DT Journal

LA Japanese

AB Drug resistance to anticancer agents is one of the major causes of cancer treatment failure. The purpose of this study was to evaluate the effect of a platelet activating factor receptor antagonist, (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,1-dimethyl-2,3,4,5-tetrahydro-8H-pyrido(4',3':4,5)thieno(3,2-f)[1,2,4]triazolo(4,3-a)[1,4]diazepine (E6123), on the sensitivity to cis-diamminedichloroplatinum (II) (CDDP) and elucidate the mechanism of the E6123-induced sensitization in a human pulmonary adenocarcinoma cell line, PC-9 and PC-9/CDDP, a CDDP-resistant subline. For PC-9 treated with E6123 at the max. concn. that did not influence cell growth, the CDDP concn. that inhibited cell growth by 50% (IC50) was 0.62+-.0.20 .mu.M, which compares to 7.57+-.0.18 .mu.M without the E6123 treatment. The sensitivity to CDDP was thus 12.2-fold enhanced by the E6123 treatment (p<0.05). For PC-9/CDDP, the IC50 to CDDP was 188.84+-.85.11 .mu.M without the E6123 treatment, whereas it was 42.08+-.25.19 .mu.M for treatment with 300 .mu.M of E6123, a 4.5-fold enhancement of sensitivity to CDDP (p<0.05). Anal. by isobologram showed that E6123 and CDDP had a synergic effect in each cell line. To assess the mechanism of sensitization by E6123, cellular platinum accumulation, intracellular glutathione content (GSH), glutathione-S-transferase activity (GST) and CDDP-induced apoptosis were evaluated. Cellular platinum accumulation was significantly higher in PC-9 cells but there was no significant change with E6123 treatment. Although GSH content and GST activity were inherently higher in PC-9/CDDP, there was no significant change caused by E6123 treatment. CDDP-induced apoptosis was enhanced by E6123 treatment in each cell line. As caspase proteases have been reported to play an important role in drug-induced apoptosis, caspase-1, caspase-2 and caspase-3 proteins were examd. by Western blotting anal. Expression of caspase-1, but not of caspase-2 and caspase-3, was enhanced by combined treatment with E6123 and CDDP in both the PC-9 and PC-9/CDDP cells. These results suggest that an overexpression of caspase-1 caused by the E6123 treatment enhances the death signal of CDDP-induced apoptosis, and that this is the mechanism of the synergic effect of E6123 and CDDP.

IT 131614-02-3, E6123

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

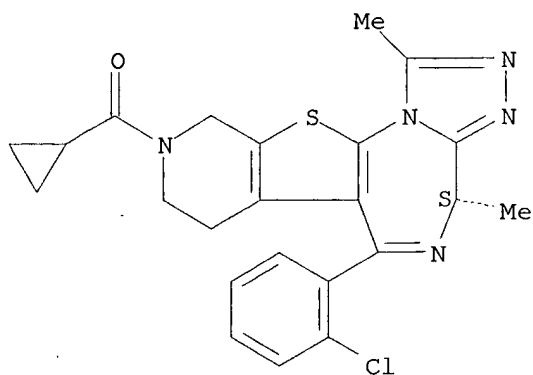
(effect of a platelet activating factor receptor antagonist on sensitivity to cis-diamminedichloroplatinum (II) in human pulmonary adenocarcinoma cell lines)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

09/701,893

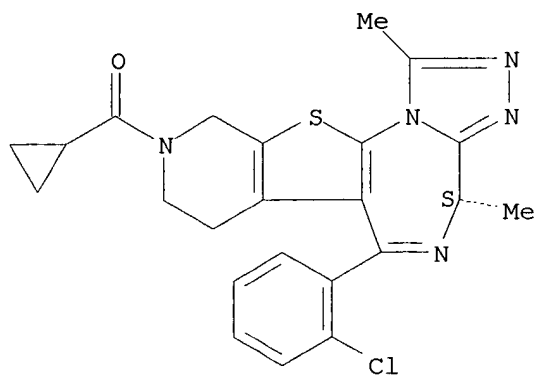
Absolute stereochemistry.



~~123~~ ANSWER 11 OF 92 CAPLUS COPYRIGHT 2001 ACS
~~AN~~ 1999:466653 CAPLUS
 DN 131:212910
 TI Possible participation of intracellular platelet-activating factor in tumor necrosis factor-.alpha. production by rat peritoneal macrophages
 AU Yamada, Masateru; Tanimoto, Atsuo; Ichinowatari, Gaku; Yaginuma, Hiroshi; Ohuchi, Kazuo
 CS Department of Pathophysiological Biochemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Miyagi, 980-8578, Japan
 SO Eur. J. Pharmacol. (1999), 374(3), 341-350
 CODEN: EJPHAZ; ISSN: 0014-2999
 PB Elsevier Science B.V.
 DT Journal
 LA English
 AB Stimulation of rat peritoneal macrophages by thapsigargin (46.1 nM) increased levels of tumor necrosis factor-.alpha. and prostaglandin E2 in the conditioned medium. Platelet-activating factor (PAF) was not detected in the conditioned medium, but the level of cell-assocd. PAF was increased transiently by thapsigargin. The PAF receptor antagonists such as E 6123 ((S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno [3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine), L-652,731 (2,5-bis(3,4,5-trimethoxyphenyl) tetrahydrofuran) and CV-6209 (2-[N-acetyl-N-(2-methoxy-3-octadecyl-carbamoyloxy propoxycarbonyl)aminomethyl]-1-ethylpyridinium chloride) inhibited thapsigargin-induced prodn. of tumor necrosis factor-.alpha.. The cyclooxygenase inhibitor indomethacin inhibited prostaglandin E2 prodn., and further enhanced thapsigargin-induced tumor necrosis factor-.alpha. prodn. in parallel with further increase in cell-assocd. PAF prodn. The enhancement of tumor necrosis factor-.alpha. prodn. induced by thapsigargin plus indomethacin was also inhibited by E 6123, L-652,731 and CV-6209. However, exogenously added PAF up to 100 nM did not stimulate prodn. of tumor necrosis factor-.alpha.. The level of tumor necrosis factor-.alpha. mRNA was increased by thapsigargin, but was lowered by the PAF receptor antagonist E 6123, suggesting that the inhibition of tumor necrosis factor-.alpha. prodn. by the PAF receptor antagonist is induced at the level of mRNA for tumor necrosis factor-.alpha.. These findings suggested that concurrently produced cell-assocd. PAF in thapsigargin-stimulated macrophages up-regulates prodn. of tumor necrosis factor-.alpha. by acting as an intracellular signaling mol. and the PAF receptor antagonists might penetrate into the cells and antagonize the action of intracellular PAF.
 IT **131614-02-3**, E 6123
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (antagonism of intracellular platelet-activating factor-mediated tumor necrosis factor-.alpha. prodn. by macrophages by)
 RN 131614-02-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



RE.CNT 44

RE

- (1) Albert, D; J Biol Chem 1983, V258, P97 CAPLUS
 - (2) Ammit, A; J Biol Chem 1997, V272, P18772 CAPLUS
 - (3) Bazan, H; Proc Natl Acad Sci USA 1993, V90, P8678 CAPLUS
 - (4) Bito, H; Eur J Biochem 1994, V221, P211 CAPLUS
 - (5) Camussi, G; J Immunol 1983, V131, P2397 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 12 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1999:319614 CAPLUS

DN 131:139146

TI A platelet activating factor receptor antagonist prevents the development of chronic arthritis in mice

AU Palacios, Itziar; Miguelez, Roberto; Sanchez-Pernaute, Olga; Gutierrez, Sylvia; Egido, Jesus; Herrero-Beaumont, Gabriel

CS Inflammation Research Laboratory, Rheumatology Division, Fundacion Jimenez Diaz, Universidad Autonoma, Madrid, 28040, Spain

SO J. Rheumatol. (1999), 26(5), 1080-1086

CODEN: JRHUA9; ISSN: 0315-162X

PB Journal of Rheumatology Publishing Co. Ltd. May

RC927.J6

DT Journal

LA English

AB We examd. the effect of treatment with the platelet activating factor (PAF) receptor antagonist BN 50730 on the clin. and morphol. evolution of collagen-induced arthritis in mice. Mice with collagen-induced arthritis were treated with BN 50730 (0.3, 1, 3 mg/kg) or vehicle (0.1% Tween-20 in saline) once a day, from 3 days before the induction of the arthritis to 70 days after. Disease evolution was followed daily by inspection of inflammatory signs and measurement of the knee joint diam. on Days 0, 40, and 70. At the end of the treatment period, the morphol. evaluation of the synovial membrane, the immunodetection of fibronectin, and the content of cartilage proteoglycans were studied. On Day 40, mice receiving the highest dose of BN 50730 (3 mg/kg) showed a redn. in the knee joint diam. in comparison with untreated (2.1 \pm 0.2 vs 2.8 \pm 0.4 mm, $p < 0.01$). On Day 70, animals receiving 1 and 3 mg/kg had a normal knee diam., while it remained enlarged in the untreated ones. In BN 50730 treated mice (3 mg/kg) we also obsd. a significant redn. of the inflammation score (0.1 \pm 0.1 vs 2.5 \pm 0.2 in the untreated) and deposition of fibronectin. Depletion of cartilage proteoglycans was also reversed with BN 50730. The beneficial effects in this model of joint injury after administration of the PAF antagonist BN 50730 suggest that PAF could be implicated in the pathogenesis of chronic arthritis.

IT 132579-32-9, BN 50730

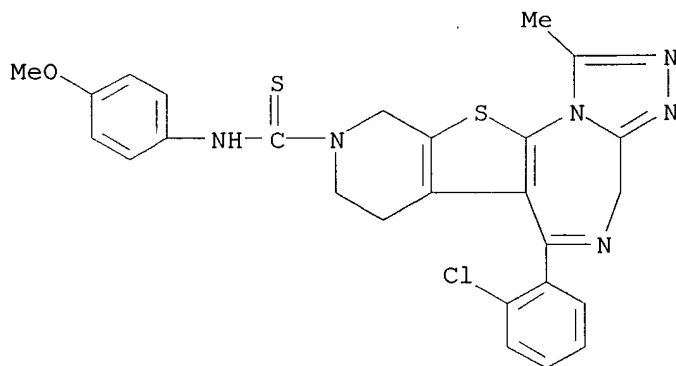
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(PAF receptor antagonist prevents chronic arthritis development)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

RE.CNT 40

RE

- (1) Bazan, H; Proc Natl Acad Sci USA 1993, V90, P8678 CAPLUS
 - (2) Bazan, N; Nature 1995, V374, P501 CAPLUS
 - (3) Bazan, N; Proc Natl Acad Sci USA 1994, V91, P5252 CAPLUS
 - (4) Braquet, P; Agents Actions 1991, V32, P34 CAPLUS
 - (5) Braquet, P; Immunol Today 1987, V8, P345 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1999:27828 CAPLUS

DN 130:66518

TI Preparation of triazolo-1,4-diazepine compounds as blood
platelet-activating factor (PAF) antagonists and thromboxane A2 (TxA2)
synthesis inhibitors and medicinal composition containing the same

IN Fujita, Masakazu; Seki, Taketsugu; Inada, Haruaki; Sano, Tetsuro

PA Nikken Chemicals Co., Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9858930	A1	19981230	WO 1998-JP2783	19980623
	W: CA, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	JP 11071378	A2	19990316	JP 1998-174494	19980622
	EP 995752	A1	20000426	EP 1998-928623	19980623
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
PRAI	JP 1997-183229		19970625		
	WO 1998-JP2783		19980623		
OS	MARPAT 130:66518				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Claimed are triazolo-1,4-diazepine compds. represented by general formula [I; R = Q; wherein A represents CO, CO-B, or B, where B represents C1-6 alkylene or C2-6 alkylene interposed by an oxygen atom; X represents N-O or CH; n is an integer of 2 to 6; R represents hydroxy or C1-6 alkyloxy or alkylamino (optionally substituted by N,N-dimethylamino, N,N-diethylamino, Ph, or heterocycle); and R1 represents hydrogen or C1-3 alkyl] and a medicine contg. the same as the active ingredients combining a PAF antagonist with a thromboxane synthesis inhibitory activity. Also claimed is a therapeutic agent for the treatment of allergic, inflammatory, ischemic, hypersecretion, and thrombotic diseases, arteriosclerosis, pulmonary hypertension, ulcers, and psoriasis. Thus, a pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine deriv. (II; R = H, R1 = Me) was condensed by 3-(4-carboxymethylphenylcarbonyl)pyridine using DCC and HOBT to give II [R = [4-(3-pyridylcarbonyl)phenyl]acetyl; R1 = Me] which underwent oximation with HONH2.HCl in ethanol in the presence of pyridine under reflux for 2 h and then treatment of the resulting oxime with NaH at room temp. for 1 h and subsequent alkylation with Et 5-bromovalerate in the presence of NaH at room temp. for 2 h to give the title compd. II (R = Q1, R1 = Me). The latter compd. at 10⁻⁷ M inhibited the PAF-induced aggregation of rabbit blood platelet by 94.6% and TxA2 synthesis from prostaglandin H2 in human blood platelet microsome by 79.6%. A tablet contg. I was prepd.

IT 218152-74-0P 218152-76-2P 218152-77-3P

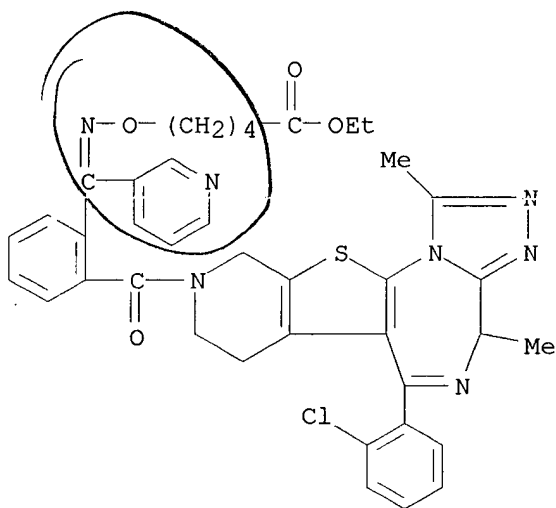
218152-78-4P 218152-79-5P 218152-80-8P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

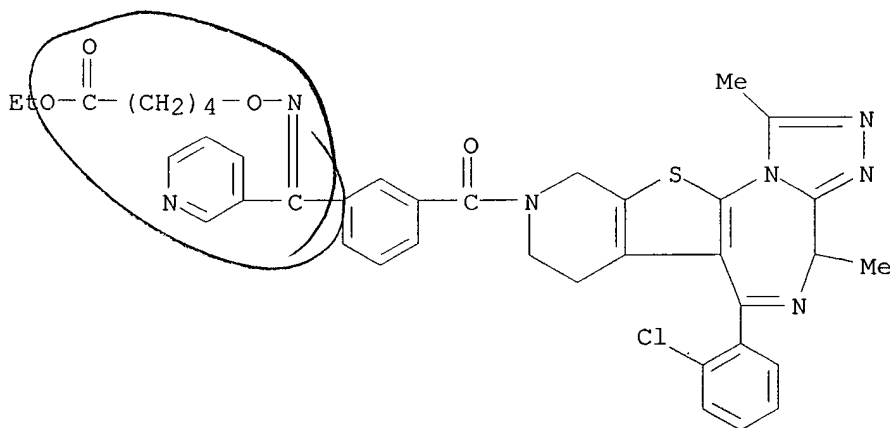
(Preparation); USES (Uses)

(prepn. of triazolo-1,4-diazepine compds. as blood platelet activating factor (PAF) antagonists and thromboxane A2 (TxA2) synthesis inhibitors)

RN 218152-74-0 CAPLUS

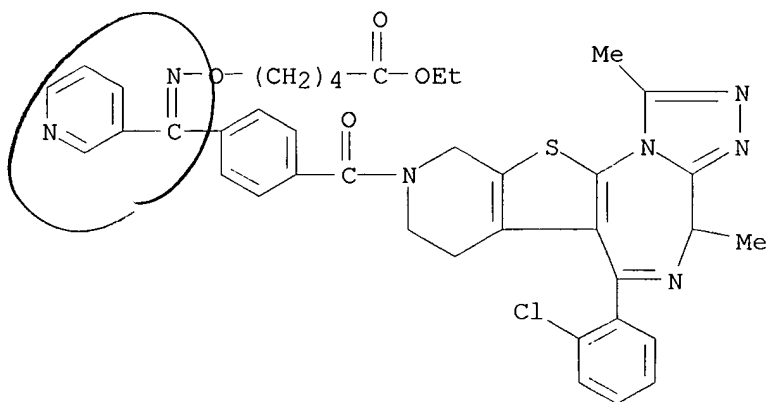
CN Pentanoic acid, 5-[[[2-[[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]carbonyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI)
(CA INDEX NAME)

RN 218152-76-2 CAPLUS

CN Pentanoic acid, 5-[[[3-[[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]carbonyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI)
(CA INDEX NAME)

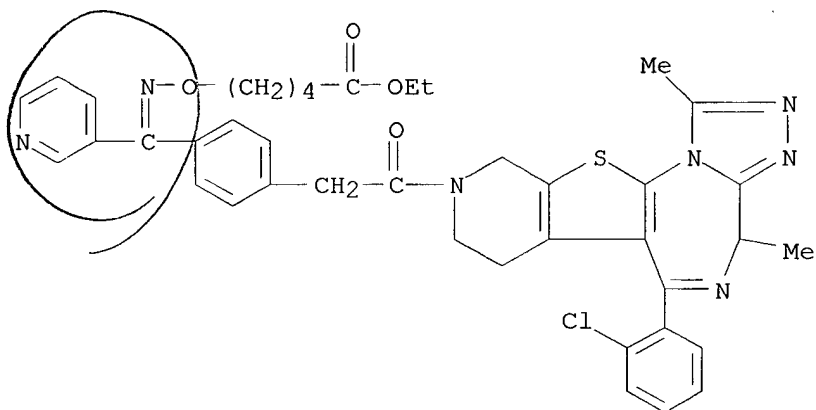
RN 218152-77-3 CAPLUS

CN Pentanoic acid, 5-[[[4-[[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]carbonyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI)
(CA INDEX NAME)



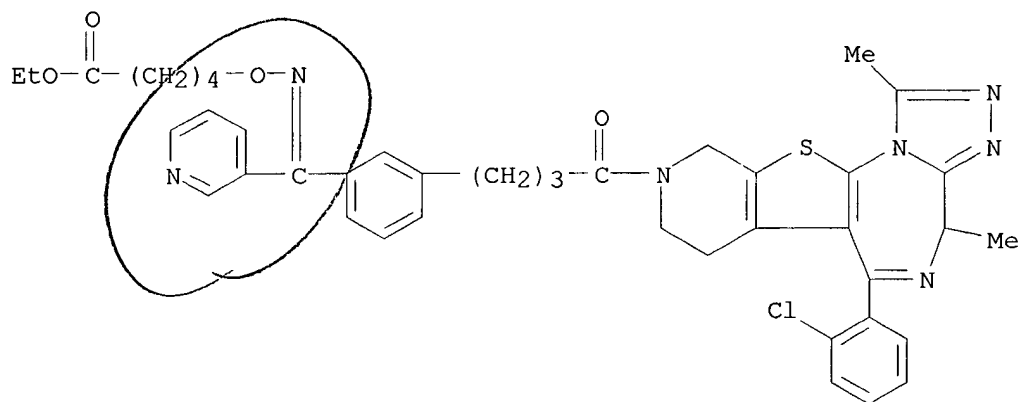
RN 218152-78-4 CAPLUS

CN Pentanoic acid, 5-[[[4-[2-[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]-2-oxoethyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI)
(CA INDEX NAME)



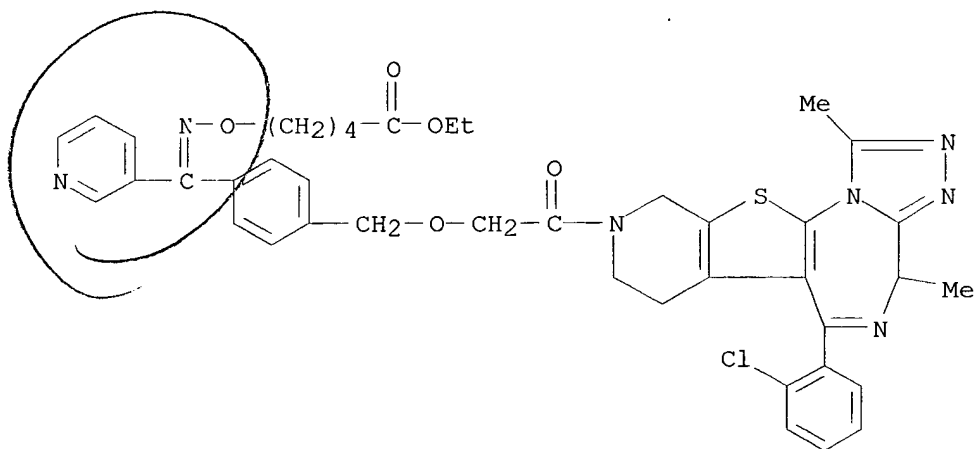
RN 218152-79-5 CAPLUS

CN Pentanoic acid, 5-[[[3-[4-[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]-4-oxobutyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI)
(CA INDEX NAME)



RN 218152-80-8 CAPLUS

CN Pentanoic acid, 5-[[[4-[[2-[6-(2-chlorophenyl)-7,10-dihydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-9(8H)-yl]-2-oxoethoxy)methyl]phenyl]-3-pyridinylmethylene]amino]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



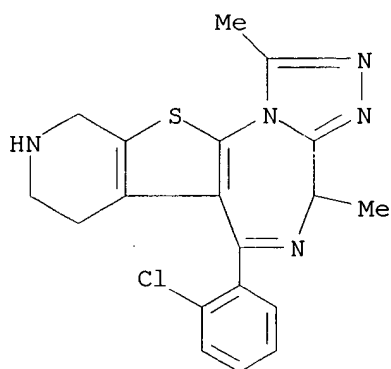
IT 130311-75-0

RL: RCT (Reactant)

(prepn. of triazolo-1,4-diazepine compds. as blood platelet activating factor (PAF) antagonists and thromboxane A2 (TxA2) synthesis inhibitors)

RN 130311-75-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX NAME)

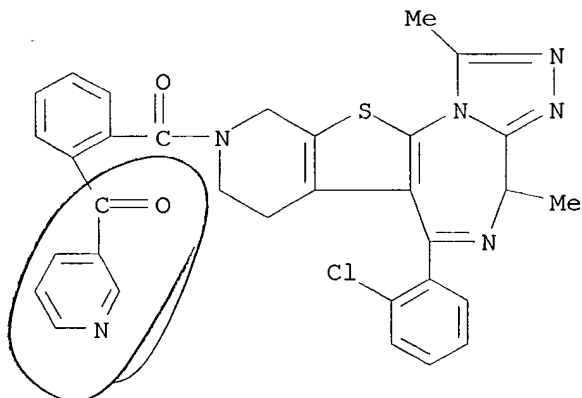


IT 218152-94-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of triazolo-1,4-diazepine compds. as blood platelet activating
factor (PAF) antagonists and thromboxane A2 (TxA2) synthesis
inhibitors)

RN 218152-94-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[2-(3-
pyridinylcarbonyl)benzoyl]- (9CI) (CA INDEX NAME)



RE.CNT 9

RE

- (1) Eisai Co Ltd; CA 2000985 A CAPLUS
 - (2) Eisai Co Ltd; EP 367110 A1 CAPLUS
 - (3) Eisai Co Ltd; US 5221671 A CAPLUS
 - (4) Eisai Co Ltd; NO 8904287 A CAPLUS
 - (6) Eisai Co Ltd; DK 8905406 A CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1998:559132 CAPLUS

DN 129:298109

TI A double blind, placebo controlled study of a platelet activating factor antagonist in patients with rheumatoid arthritis

AU Hilliquin, Pascal; Chermat-Izard, Valerie; Menkes, Charles-Joel

CS Institut de Rhumatologie, Hopital Cochin, Paris, 75679, Fr.

SO J. Rheumatol. (1998), 25(8), 1502-1507

CODEN: JRHUA9; ISSN: 0315-162X

PB Journal of Rheumatology Publishing Co. Ltd.

DT Journal

LA English

AB Our objective was to evaluate the efficacy and tolerance of a platelet activating factor-acether (PAF) antagonist, BN 50730, in patients with rheumatoid arthritis (RA). A total of 56 patients with active RA were enrolled in a multicenter, double blind, placebo controlled study of BN 50730. Patients received either BN 50730 (40 mg orally bid) or placebo for 84 days. Treatment with BN 50730 resulted in no improvement and was no more effective than placebo in improving clin. and biol. indexes of RA activity. Adverse events were obsd. in the 2 treatment groups, and BN 50730 was generally well tolerated. PAF antagonist BN 50730 at a daily dose of 80 mg was ineffective in the treatment of RA.

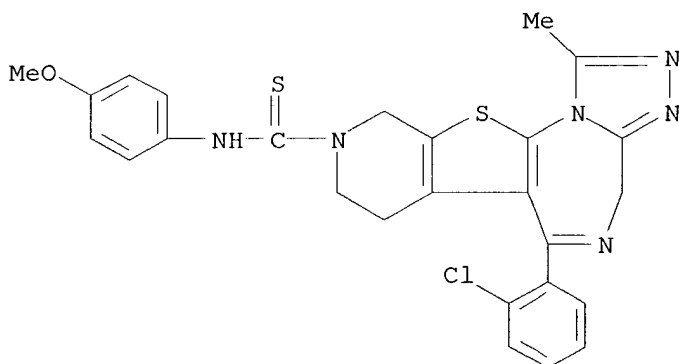
IT 132579-32-9, BN 50730

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(platelet activating factor antagonist in humans with rheumatoid arthritis)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



~~123~~ ANSWER 15 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1998:232246 CAPLUS

~~DN~~ 129:23204

TI Effect of synthetase inhibitors and receptor antagonists in antigen-induced contraction of human lung parenchyma

AU Fukushima, Chizu; Shimoda, Terufumi; Matsuse, Hiroto; Matsuo, Nobuko; Takao, Atsuko; Obase, Yasusi; Kohno, Shigeru; Asai, Sadahiro

CS Second Dep. Internal Medicine, Nagasaki Univ. Sch. Med., Sasebo City, Japan

SO Ann. Allergy, Asthma, Immunol. (1998), 80(3), 245-250

CODEN: ALAIF6; ISSN: 1081-1206

PB American College of Allergy, Asthma, & Immunology

DT Journal

LA English

AB Chem. mediators induce bronchoconstriction, enhance vascular permeability, and promote inflammation. The use of synthetase inhibitors and receptor antagonists of these mediators may be useful in the treatment of asthma. We evaluated the role of chem. mediators in mite antigen-induced contraction in resected human lung parenchyma using synthetase inhibitors and receptor antagonists for these mediators. Thromboxane A2 (TXA2) synthetase inhibitors significantly inhibited TXB2 release but not contraction. The magnitude of the inhibitory effect was in the order of LT receptor antagonist > 5-lipoxygenase inhibitor > TXA2 receptor antagonist > PAF antagonist, TXA2 synthetase inhibitor, antihistamine > cyclooxygenase inhibitor. Among chem. mediators, LT appears to be the most closely involved in the immediate antigen-induced contractile response in resected human lung parenchyma. Receptor antagonists produced a more marked inhibition of antigen-induced contraction than synthetase inhibitors.

IT **131614-02-3**, E-6123

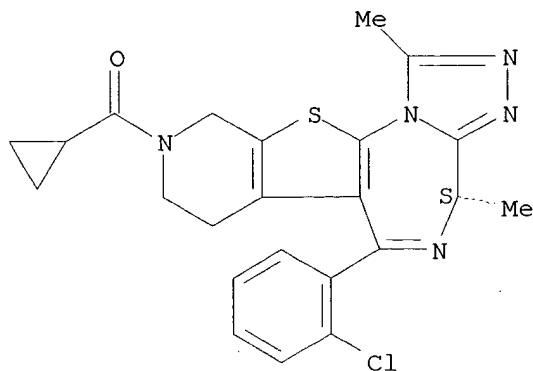
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(synthetase inhibitors and receptor antagonists effect in antigen-induced contraction of human lung parenchyma)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 16 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1998:114469 CAPLUS

DN 128:228965

TI Effects of BN-50730 (PAF receptor antagonist) and physostigmine (AChE inhibitor) on learning and memory in mice

AU Singh, Nirmal; Sharma, Ajay; Singh, Manjeet

CS Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, India

SO Methods Find. Exp. Clin. Pharmacol. (1997), 19(9), 585-588
CODEN: MFEPDX; ISSN: 0379-0355

PB J. R. Prous, S.A.

DT Journal

LA English

AB The present study was designed to investigate the effect of BN-50730, a PAF receptor antagonist, on learning and memory in mice using elevated plus-maze and to delineate the role of acetylcholine in modulating the effect of PAF receptor antagonist on learning and memory. BN-50730 administered immediately after plus-maze training on day 1 induced retrograde amnesia as indicated by a dose-dependent increase in transfer latency (TL) measured on day 2 whereas no such increase in TL was noted when BN-50730 (2.5 mg/kg, i.p.) was administered prior to plus-maze training. Physostigmine (0.5 mg/kg; 1.0 mg/kg, i.p.) administered 30 min prior to plus-maze training attenuated BN-50730-induced increase in TL measured on day 2. These results suggest that BN-50730, a PAF receptor antagonist, produced retrograde amnesia and physostigmine attenuated BN-50730-induced amnesia possibly through increased concn. of cerebral acetylcholine and a consequent increase in PAF release.

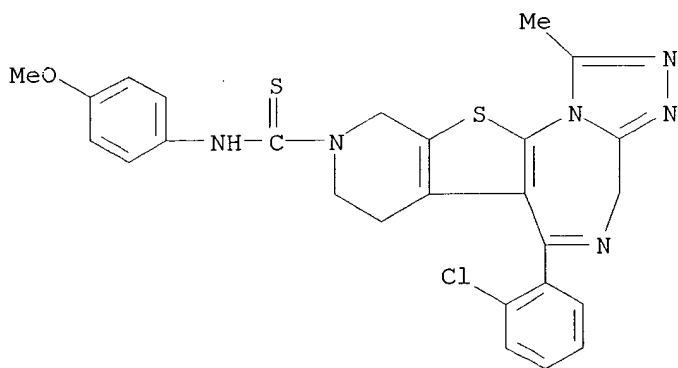
IT **132579-32-9**, BN-50730

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

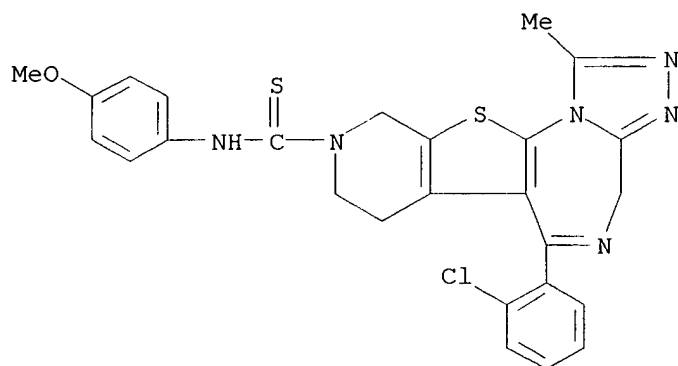
(BN-50730 (PAF receptor antagonist) and physostigmine (AChE inhibitor) effect on learning and memory)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 17 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1998:45006 CAPLUS
DN 128:84216
TI Possible mechanism of alprazolam-induced amnesia in mice
AU Singh, Nirmal; Sharma, Ajay; Singh, Manjeet
CS Dep. Pharmaceutical Sciences Drug Research, Punjabi Univ., Patiala,
147002, India
SO Pharmacology (1998), 56(1), 46-50
CODEN: PHMGBN; ISSN: 0031-7012
PB S. Karger AG
DT Journal
LA English
AB Alprazolam produced anterograde as well as retrograde amnesia in mice
assessed using elevated plus-maze. Flumazenil (10 mg/kg i.p.) attenuated
anterograde and retrograde amnesia produced by alprazolam. It is proposed
that anterograde amnesia produced by alprazolam may be mediated through
the activation of benzodiazepine receptors. Retrograde amnesia of
alprazolam may be mediated through the blockade of PAF receptors.
Moreover, flumazenil facilitates learning and memory perhaps by modulating
the release of PAF and consequently attenuated alprazolam and
BN-50730-(PAF receptor antagonist)-induced retrograde amnesia.
IT **132579-32-9**, BN-50730
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(possible mechanism of alprazolam-induced amnesia in mice)
RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 18 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1997:559720 CAPLUS

DN 127:242642

TI Inflammatory signaling pathways in pharmacology of cerebral ischemia

AU Bazan, N. G.

CS Neuroscience Center of Excellence, Louisiana State University Medical Center School of Medicine, New Orleans, LA, 70112, USA

SO Pharmacol. Cereb. Ischemia 1996, [Int. Symp.], 6th (1996), 173-180.

Editor(s): Krieglstein, Josef. Publisher: Medpharm Scientific Publishers, Stuttgart, Germany.

CODEN: 64YHA7

DT Conference; General Review

LA English

AB A review with 28 refs. The brain's responses to ischemia and seizure initially include membrane depolarization, enhanced accumulation of phospholipase A2 products such as arachidonic acid and PAF, glutamate release, and influx of calcium ions. The phospholipase A2 pathway represents a neural inflammatory response by which bioactive lipids become injury signals in ischemia-reperfusion, as well as during repeated seizures, thus promoting brain damage. The inflammatory mediator PAF is a transcriptional activator of COX-2; BN50730, an intracellular PAF antagonist, blocks this effect. Therefore, we tested the in vivo effectiveness of BN50730 in blocking COX-2 induction. A single intracerebro-ventricular injection of BN50730 prevents kainic acid-triggered COX-2 increase in hippocampus. COX-2 accumulation may be triggered by PAF. It is of interest that COX-2 enhanced expression precedes neuronal damage. Thus COX-2, a gene involved in synaptic plasticity responses, may initiate pathol. forms of neuroplasticity. Therefore, the PAF/COX-2 pathway is a new drug target in the brain's inflammatory response to ischemia.

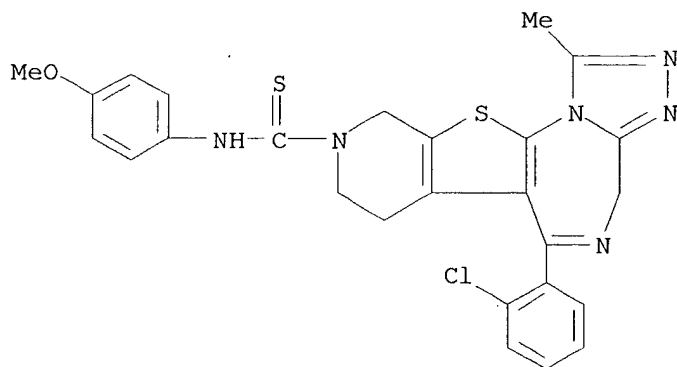
IT 132579-32-9, BN50730

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

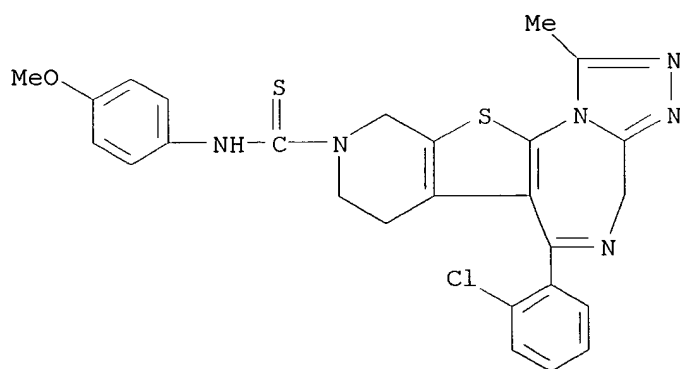
(inflammatory signaling pathways in pharmacol. of cerebral ischemia: PAF/COX-2 pathway as new drug target)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 19 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1997:91715 CAPLUS
 DN 126:195206
 TI Experimental electroretinographic exploration of retinal ischemia: preventive use of free radical scavengers and anti-PAF agents
 AU Menerath, J. M.; Cluzel, J.; Droy-Lefaix, M. Th.; Doly, M.
 CS Facultes de Medecine et de Pharmacie, Laboratoire de Biophysique, INSERM, Clermont-Ferrand, Fr.
 SO J. Ocul. Pharmacol. Ther. (1997), 13(1), 81-88
 CODEN: JOPTFU; ISSN: 1080-7683
 PB Liebert
 DT Journal
 LA English
 AB Electoretinog. exploration is an effective approach to evaluate retinal function. To investigate physiopathol. mechanisms and evaluate potentially protective therapies for retinal ischemia, the authors developed three exptl. models: the first two on isolated retina, with ischemia induced by either stopping perfusion or clamping the ophthalmic artery, and the third, in vivo, with ischemia induced by ocular hypertonia. Since free radicals are implicated in the formation of post-ischemic lesions, the authors evaluated the protective effects of drugs known to be free radical scavengers and of an immunomediator antagonist, an anti-PAF (platelet activating factor) agent. The radical scavengers and the anti-PAF agent appear to be valuable in the prevention of retinal impairment in retinal ischemia.
 IT **132579-32-9**, BN 50730
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (exptl. electroretinog. exploration of retinal ischemia and preventive use of free radical scavengers and anti-PAF agents in relation to pathophysiol. mechanism)
 RN 132579-32-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



~~DI~~3 ANSWER 20 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1996:707122 CAPLUS

DN 126:42196

TI Purification and characterization of rhesus monkey liver amido hydrolases and their roles in the metabolic polymorphism for E6123, a platelet-activating factor receptor antagonist

AU Kusano, Kazutomi; Seko, Takayuki; Tanaka, Shigeru; Shikata, Yasushi; Ando, Tomomi; Ida, Satoshi; Hosokawa, Masakiyo; Satoh, Tetsuo; Yuzuriha, Teruaki; Hori, Toru

CS Drug Metabolism Research Section, Chiba Univ., Ibaraki, 300-26, Japan

SO Drug Metab. Dispos. (1996), 24(11), 1186-1191

CODEN: DMDSAL; ISSN: 0090-9556

PB Williams & Wilkins

DT Journal

LA English

AB We previously showed that a polymorphism for E6123 [(S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine] metab. exists only in rhesus monkeys. In the present study, we purified, from rhesus monkey hepatic microsomes, three amido hydrolases that are involved in the metabolic polymorphism,. Two forms of amido hydrolase from an extensive metabolizer and one from a poor metabolizer were purified by Q-Sepharose Fast Flow, Red A-agarose, octylamino-Sepharose 4B, and hydroxyapatite-Ultrogel chromatog., after solubilization with Lubrol. The three purified enzymes had the same mol. mass (47 kDa), and their amino-terminal amino acid sequences were identical. The enzymes were different from various known carboxylesterases in terms of substrate specificity, mol. mass, and amino-terminal amino acid sequence. They resembled arylacetamide deacetylase from human hepatic microsomes with respect to mol. mass and amino-terminal amino acid sequence. The KM values of the high and low affinity enzymes in the extensive metabolizer and the sole enzyme in the poor metabolizer were 37.6, 73.0, and 76. .mu.M, resp. The Vmax values were 3312.4, 504.8, and 427.9 pmol/min/mg of protein, resp. The high affinity enzyme in extensive metabolizer appears to be quite distinct, whereas the low affinity enzyme in extensive metabolizer is similar or identical to the sole enzyme in poor metabolizer. Thus, the metabolic polymorphism in rhesus monkey may depend upon the existence of the high affinity enzyme in extensive metabolizer.

IT 131614-02-3, E6123

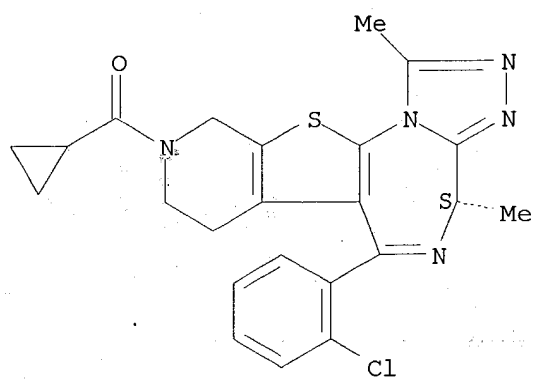
RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (purifn. and characterization of rhesus monkey liver amido hydrolases and their roles in the metabolic polymorphism for E6123)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



~~L23~~ ANSWER 21 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1996:699203 CAPLUS

~~DN~~ 125:316898

TI Involvement of PAF in post-allergic propranolol-induced bronchoconstriction in guinea pigs

AU Fujimura, M.; Tsujiura, M.; Songur, N.; Myou, S.; Matsuda, T.

CS School Medicine, Kanazawa University, Kanazawa, 920, Japan

SO Eur. Respir. J. (1996), 9(10), 2064-2069

CODEN: ERJOEI; ISSN: 0903-1936

DT Journal

LA English

AB Administration of propranolol can provoke bronchoconstriction in asthmatic patients. Recently, we successfully developed a guinea-pig model for propranolol-induced bronchoconstriction (PIB). We hypothesized that such bronchoconstriction may result from the inflammatory mediators released by an allergic reaction. The purpose of this study was to examine the role of platelet-activating factor (PAF) in the development of PIB after allergic reaction. Propranolol, at a concn. of 10 mg.cntdot.mL⁻¹ was inhaled 20 min after antigen challenge in passively sensitized, anesthetized and artificially-ventilated guinea pigs. The animals were treated i.v. with PAF antagonists, E6123 (1 and 10 .mu.g.cntdot.kg⁻¹) or Y-24180 (1 and 10 mg.cntdot.kg⁻¹), 10 min before or 15 min after antigen challenge. Propranolol inhaled 20 min after antigen challenge caused bronchoconstriction. E6123 and Y-24180 administered 15 min after antigen challenge as well as 10 min before antigen challenge reduced the PIB in a dose-dependent manner. We conclude that platelet-activating factor may contribute to the development of propranolol-induced bronchoconstriction after allergic reaction in our guinea pig model.

IT **131614-02-3**, E6123

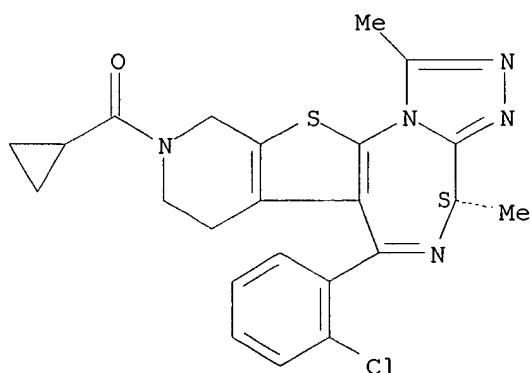
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(PAF involvement in post-allergic propranolol-induced bronchoconstriction in guinea pigs)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/701,893

~~L2~~ ANSWER 22 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1996:658170 CAPLUS

DN 126:84063

TI Molecular modeling on platelet-activating factor (PAF) and new proposed PAF antagonists

AU De Santa'anna, Carlos M. R.; De Alencastro, Ricardo Bicca; Fraga, Carlos A. M.; Barreiro, Eliezer J.; Da Motta Neto, Joaquim Delphino

CS Physical Organic Chem. Group, Departamento de Quimica Organica, Instituto de Quimica da UFRJ, Cidade Universitaria, Rio de Janeiro, 31949-900, Brazil

SO Int. J. Quantum Chem. (1996), 60(5), 1069-1080

CODEN: IJQCB2; ISSN: 0020-7608

PB Wiley

DT Journal

LA English

AB Platelet-activating factor (PAF) is an autocoid derived from cellular membrane phospholipids in response to chem. or phys. stimuli. It has been identified as 1-O-alkyl-2-acetyl-sn-glycerol-3-phosphocholine; the alkyl group is composed of 16 or 18 carbon atoms in human cells. PAF can cause a series of pathophysiol. effects, related to inflammatory and allergic diseases such as asthma, gastric ulcerations, transplant rejections, psoriasis, cerebral, renal, and myocardial ischemia. As PAF biol. action is a result of interactions with specific receptors on target cells, several specific PAF receptor antagonists have been proposed for therapeutic control of the pathol. states in which PAF is implicated. In this work we have calcd. at Aml level 16 conformations of a model (alkyl = octyl) of (R)-PAF. We have used these conformations and calcd. structures of two hexazepines (WEB 2086 and E 6123), FR 128998 and RP 59227, known antagonists of PAF activity currently under development, to test a recently proposed pharmacophore map. Our results suggest that the model is too rigid. Having this in mind, we used the pharmacophore model to evaluate the potential activity of a new series of proposed PAF receptor antagonists based on bicyclo[3.3.0]-2-oxaoctane. The results were used to decide which compds. should receive priority in synthesis. The synthetic results and pharmacol. profiles of the new derivs. will be published elsewhere.

IT 131614-02-3, E 6123

RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

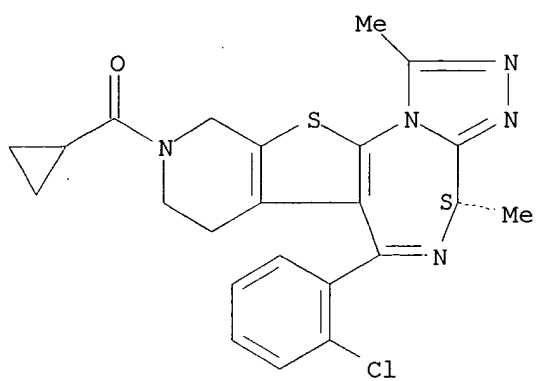
(mol. modeling on platelet-activating factor and new proposed PAF antagonists)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



L23 ANSWER 23 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1996:253280 CAPLUS

DN 124:331482

TI Determination of the anti-platelet-activating factor BN-50727 and metabolites in human urine by high-performance liquid chromatography using solid-phase extraction

AU Prunonosa, J.; Sola, J.; Peraire, C.; Pla, F.; Laverne, O.; Obach, R.

CS Pharmacokinetic Department, S. A. Lasa Laboratories, Barcelona, Spain

SO J. Chromatogr., B: Biomed. Appl. (1996), 677(2), 388-92

CODEN: JCBBEF; ISSN: 0378-4347

DT Journal

LA English

AB A sensitive and selective HPLC solid-phase extn. procedure was developed for the detn. of platelet-activating factor antagonist BN-50727 and its metabolites in human urine. The procedure consisted in a double solid-phase extn. of the urine samples on cyanopropyl and silica cartridges, followed by an automated solid-phase extn. of the drug and metabolites on CBA cartridges and posterior elution online to the chromatog. system for its sepn. The method allowed quantitation in the concn. range 10-2400 ng/mL urine for both BN-50727 and the main metabolite, the O-demethylated BN-50727 product. The limit of quantitation for both compds. was 10 ng/mL. The inter-assay precision of the method, expressed as relative std. deviation, ranged from 1.9 to 4.5% for BN-50727 and from 2.5 to 9.0% for the metabolite. The accuracy, expressed as relative error, ranged from -2.4 to 4.2% and from 0.2 to 6.2%, resp. This paper describes the validation of the anal. methodol. for the detn. of BN-50727 in human urine and also for its metabolites. The method has been used to follow the time course of BN-50727 and its metabolites in human urine after single-dose administration.

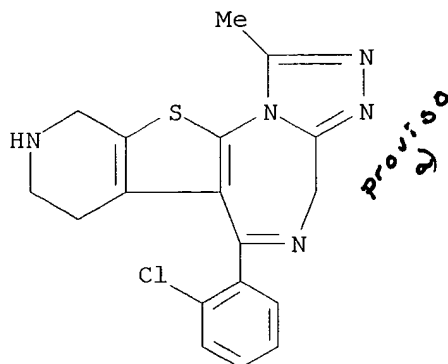
IT **114800-58-7**, NHPTT **132418-35-0**, BN-50727**165898-01-1**

RL: ANT (Analyte); ANST (Analytical study)

(detn. of anti-platelet-activating factor BN-50727 and metabolites in human urine by high-performance liq. chromatog. using solid-phase extn.)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

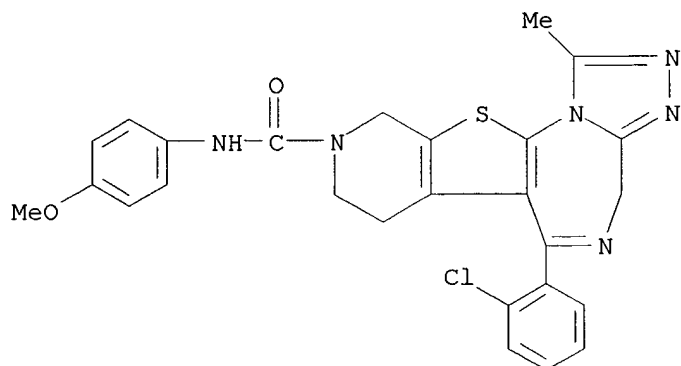


RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-

09/701,893

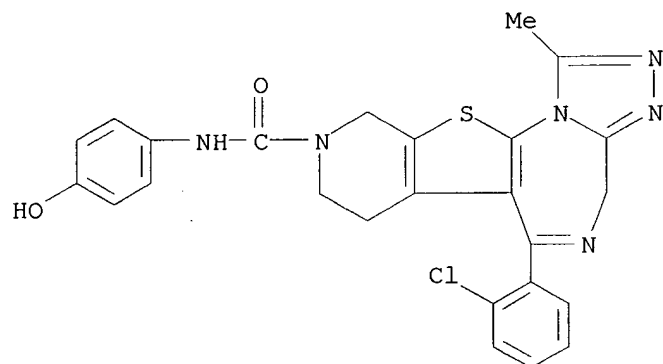
methyl- (9CI) (CA INDEX NAME)



6:

RN 165898-01-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



6:

L23 ANSWER 24 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1996:174217 CAPLUS

DN 124:270259

TI Existence of two basic sites in triazolo-1,4-diazepines: determination of two pKa values for a model compound in water

AU Legouin, Beatrice; Burgot, Jean-Louis

CS UFR Sciences Pharmaceutiques Biologiques, Laboratoire Chimie Analytique, Rennes, 35043, Fr.

SO Analyst (Cambridge, U. K.) (1996), 121(1), 43-8

CODEN: ANALAO; ISSN: 0003-2654

DT Journal

LA English

AB By a UV/VIS spectrophotometric study in the pH range -1.6 to 10.1 and by a polarog. study of a water sol. model compd., the occurrence of two basic sites in water has been ascertained for triazolo-1,4-diazepines. The pKa values found for this model were -0.24 and +1.81. Owing to the overlapping of the two pKa values, microforms exist simultaneously. Corresponding ionization microconstant values have been tentatively assigned.

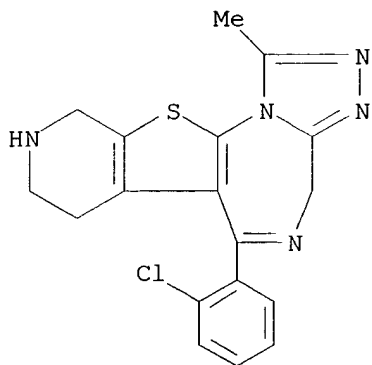
IT 114800-58-7, NHPTT

RL: PRP (Properties)

(existence of two basic sites in triazolo-1,4-diazepines: detn. of two pKa values for a model compd. in water)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 25 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1996:51752 CAPLUS

DN 124:164644

TI Formation of a highly stable complex between BN 50730 [4,7,8,10-tetrahydro-1-methyl-6-(2-chlorophenyl)-9-(4-methoxyphenylcarbamoyl)-[4',3'-4,5]pyrido[3,2-f]thieno-1,2,4-triazolo[4,3-a]-1,4-diazepine] and the platelet-activating factor receptor in rabbit platelet membranes

AU Silva, Claudia L. M.; Cruz, Hermenegildo N.; Violante, Flavio A.; Cordeiro, Renato S. B.; Martins, Marco A.; Noeel, Francois

CS Instituto Ciencias Biomedicas, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 21941-590, Brazil

SO Biochem. Pharmacol. (1996), 51(2), 193-6
CODEN: BCPCA6; ISSN: 0006-2952

DT Journal

LA English

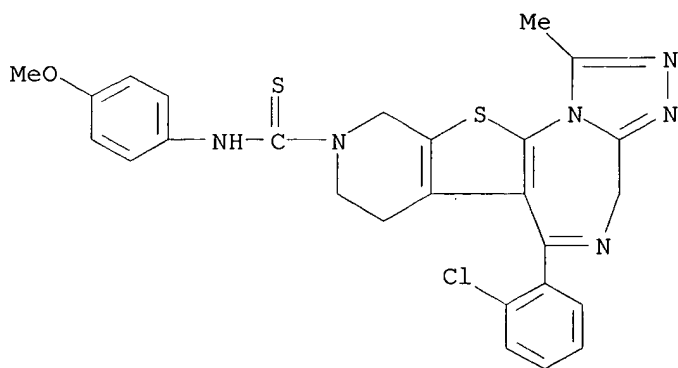
AB BN 50730 [4,7,8,10-tetrahydro-1-methyl-6-(2-chlorophenyl)-9-(4-methoxyphenylcarbamoyl)-[4',3'-4,5]pyrido[3,2-f]thieno-1,2,4-triazolo[4,3-a]-1,4-diazepine], a novel platelet-activating factor (PAF) receptor antagonist with a tetrazepine structure, decreased the maximal no. of binding sites (Bmax) of [³H]PAF in rabbit platelet membranes without altering its dissociation constant. Platelet aggregation induced by 1 μM PAF was prevented by preincubation with 1 μM BN 50730. The washing of the platelets preincubated with BN 50730 failed to revert its inhibitory effects. We conclude that BN 50730 acts as a non-competitive antagonist of the PAF receptor, due to the formation of a highly stable drug-receptor complex.

IT 132579-32-9, BN 50730

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(BN 50730-PAF receptor complex formation in rabbit platelet membranes)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 26 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1996:30329 CAPLUS

DN 124:164620

TI Anti-inflammatory effect of a PAF receptor antagonist and a new molecule with antiproteinase activity in an experimental model of acute urate crystal arthritis

AU Miguelez, Roberto; Palacios, Itziar; Navarro, Francisco; Gutierrez, Sylvia; Sanchez-Pernaute, Olga; Egido, Jesus; Gonzalez, Eva; Herrero-Beaumont, Gabriel

CS Inflammation Unit, Servicio de Reumatologia, Fundacion Jimenez Diaz, Avda Reyes Catolicos 2, Madrid, 28040, Spain

SO J. Lipid Mediators Cell Signalling (1996), 13(1), 35-49
CODEN: JLMSEO; ISSN: 0929-7855

DT Journal

LA English

AB Platelet activating factor (PAF) is a potent mediator of allergic and inflammatory reactions in different pathol. conditions. During recent years there has been increasing evidence that PAF can play an important role in the pathogenesis of arthritis. The PMN proteinases make an important contribution to the final tissue joint destruction in arthritis. In a rabbit model of acute crystal arthritis, we have compared the anti-inflammatory effect of two new mols.: BN 50727 with anti-PAF activity, and BN 50548 an inhibitor of PMN proteinases. These mols. were administered dissolved in DMSO at doses of 6 mg/kg three times daily i.p., beginning 24 h before the induction of arthritis. Compared with the untreated animals those receiving the drugs, presented a significant diminution in: (1) the synovial fluid vol.; (2) the amt. of cells infiltrating the joint cavity and the synovial membrane; and (3) the PGE2 concn. Furthermore, in both groups of treated rabbits there was a significant decrease in synovial IL-6 concn. and in C-reactive protein serum levels and an important decline of histopathol. score. The treatment with BN 50548 induced a significant redn. of TNF levels in the synovial fluid vs DMSO-treated and untreated rabbits. These results further strengthen that in an acute exptl. arthritis model, mols. with capacity to antagonize the in vivo action of PAF have an anti-inflammatory effect reflecting an important role for this mediator in the pathogenesis of arthritis. We have also seen that an inhibitor of proteinases is capable of improving the joint inflammation apparently through a decrease in tumor necrosis factor (TNF) and interleukin-6 (IL-6) synovial levels. Furthermore, the proteinase inhibitor treatment preserves the loss of articular proteoglycan content, in an acute arthritis model. In conclusion, BN 50727 and BN 50548, two compds. with PAF antagonist and antiproteinase activity, resp. exert an anti-inflammatory effect in an exptl. model of acute urate crystal arthritis, probably due to a decrease in TNF.alpha. and IL-6 synthesis.

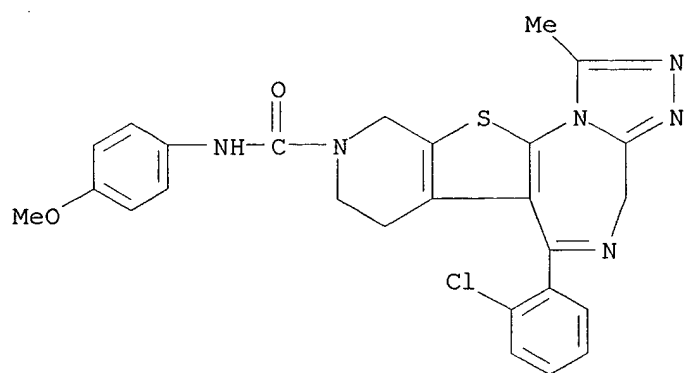
IT 132418-35-0, BN 50727

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory effect of PAF receptor antagonist BN 50727 and proteinase inhibitor BN 50548 in acute arthritis)

RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 27 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:809432 CAPLUS

DN 123:217976

TI Treatment of rheumatoid arthritis with platelet activating factor antagonist BN 50730

AU Hilliquin, Pascal; Guinot, Philippe; Chermat-Izard, Valerie; Puechal, Xavier; Menkes, Charles-Joeel

CS Service de Rhumatologie A, Hopital Cochin, Paris, Fr.

SO J. Rheumatol. (1995), 22(9), 1651-4

CODEN: JRHUA9; ISSN: 0315-162X

DT Journal

LA English

AB The objective was to det. the efficacy and safety of a platelet activating factor (PAF) antagonist, BN 50730, in patients with rheumatoid arthritis. Ten patients with an active disease were treated for 4 wk with a PAF receptor antagonist, BN 50730, given orally (40 mg twice daily). The treatment period was followed by a 4 wk followup period. Clin. indicators of disease activity significantly improved during the treatment period, with a progressive return to baseline values during the followup period. No significant change in lab. variables was obsd. The tolerance of the treatment was excellent, and no clin. or lab. evidence of side effects was recorded. These results need to be confirmed in a controlled study, but suggest an antiinflammatory effect. PAF antagonists could represent a new class of therapeutic agents in inflammatory arthropathies.

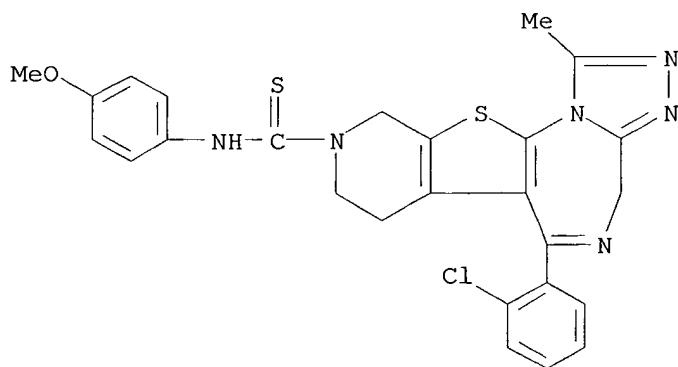
IT 132579-32-9, BN 50730

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of rheumatoid arthritis with platelet activating factor antagonist BN 50730 in humans)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 28 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:701238 CAPLUS

DN 123:132410

TI PAF antagonists block induction of nitric oxide synthase in cultured macrophages and vascular smooth muscle cells

AU Arthur, Jane F.; Shahin, Susan; Disting, Gregory J.

CS Department of Physiology, University of Melbourne, Parkville, Australia

SO Clin. Exp. Pharmacol. Physiol. (1995), 22(6/7), 452-4

CODEN: CEXPB9; ISSN: 0305-1870

DT Journal

LA English

AB Nitric oxide (NO) synthase inhibitors and PAF antagonists abrogate hypotension in septic shock. The latter may act by blocking intracellular transduction mechanisms in vascular smooth muscle cells and inflammatory cells. We examd. the effect of PAF antagonists on expression of inducible NO synthase. A murine macrophage cell line (J774.2) and rat vascular smooth muscle cells (VSMC) were stimulated with lipopolysaccharide (LPS), either alone or in combination with PAF or PAF antagonists, BN 50739 or E-6123. NO synthase activity in J774.2 was measured by the conversion of [3H] L-arginine to [3H] L-citrulline. Nitrite accumulation was measured in the culture medium of J774.2 and VSM. BN 50739 (10 .mu.mol/L) and E-6123 (1 .mu.mol/L) both reduced the expression of calcium-independent NO synthase activity and nitrite accumulation, while PAF alone had no effect. Inhibition of NO synthase induction by PAF antagonists might afford therapeutic benefits in the management of septic shock and possibly other cardiovascular disorders.

IT 128672-07-1, Bn 50739 131614-02-3, e 6123

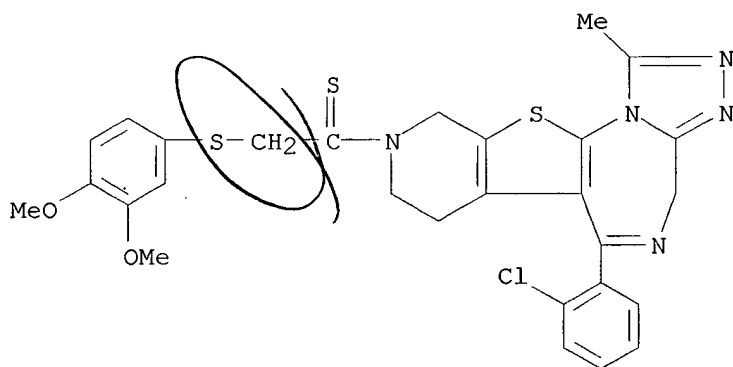
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(PAF antagonists block induction of nitric oxide synthase in cultured macrophages and vascular smooth muscle cells)

RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

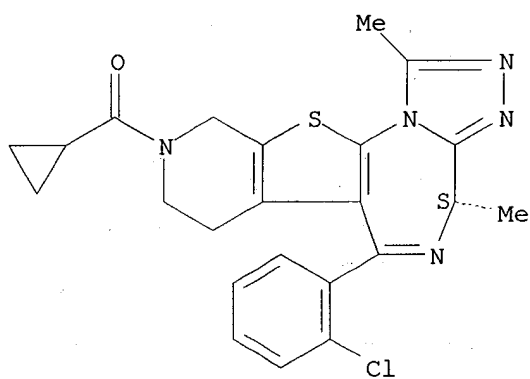


RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



L23 ANSWER 29 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:670503 CAPLUS

DN 123:102202

TI Protective effect of a specific PAF antagonist on vincristine-induced experimental retinopathy

AU Doly, Michel; Cluzel, Jacques; Bonhomme, Brigitte; Millerin, Martine; Braquet, Pierre

CS Laboratoire de Biophysique, Facultes de Medecine et de Pharmacie, Clermont-Ferrand, 63001/1, Fr.

SO Acta Ophthalmol. Scand. (1995), 73(2), 155-7

CODEN: AOSCFV; ISSN: 1395-3907

PB Scriptor

DT Journal

LA English

AB The alkaloid vincristine displays considerable toxicity, particularly for the retina. This type of retinopathy being an inflammatory disease, we measured the effects of a new hetrazepine platelet activating factor antagonist, BN 50730, on a vincristine-induced retinopathy in the rat. Retinal impairments were established by recording several parameters of the electroretinogram obtained from isolated retina. Our results indicate that (1) the increase in PIII duration induced by vincristine is significantly reduced by BN 50730 administration (2) the decrease in the amplitude of the PIII/b wave ratio caused by vincristine is partially inhibited by treatment with BN 50730. These expts. suggest that platelet activating factor is implicated in vincristine retinopathy and demonstrate the therapeutic effect of a specific antagonist of the mediator.

IT **132579-32-9**, BN50730

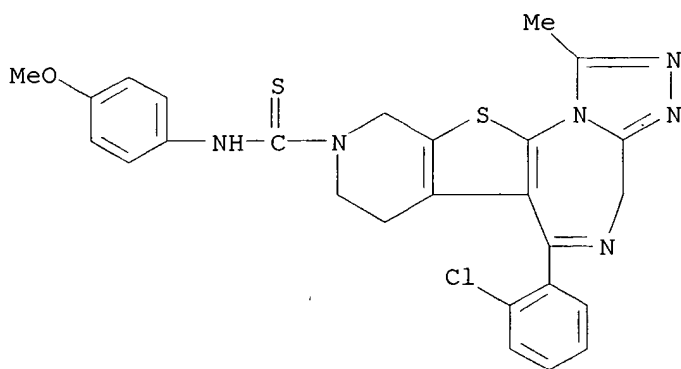
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(protective effect of a specific PAF antagonist on vincristine-induced exptl. retinopathy)

RN 132579-32-9 CAPLUS

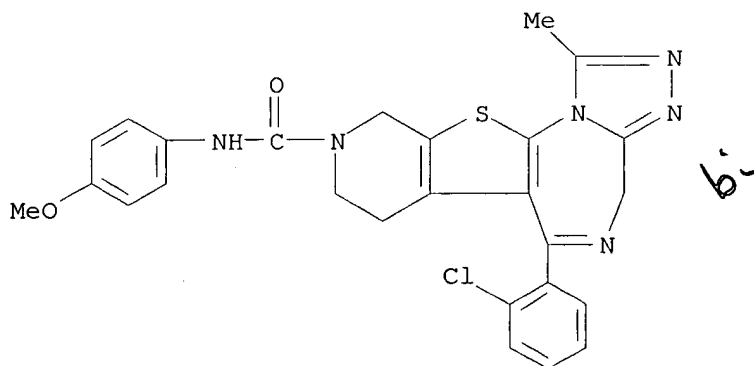
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



502 23 892

L23 ANSWER 30 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1995:655734 CAPLUS
 DN 123:101881
 TI Determination of the anti-platelet-activating factor BN-50727 and its metabolites in human plasma by high-performance liquid chromatography-solid-phase extraction
 AU Prunonosa, J.; Parera, L.; Peraire, C.; Pla, F.; Lavergne, O.; Obach, R.
 CS Pharmacokinetic Department, S.A. Lasa Laboratorios, Crta. Laurea Miro 395, Sant Feliu de Llobregat, Barcelona, 08980, Spain
 SO J. Chromatogr., B: Biomed. Appl. (1995), 668(2), 281-90
 CODEN: JCBBEP
 DT Journal
 LA English
 AB A sensitive and selective HPLC-solid-phase extn. procedure was developed for the detn. of platelet-activating factor antagonist BN-50727 and its metabolites in human plasma. The procedure consisted of an automated solid-phase extn. of the drug and metabolites on disposable propylcarboxylic acid cartridges, followed by online chromatog. sepn. The method was linear over the range 3.75-2400 ng/mL, and the limit of quantitation for BN-50727 in plasma was 3.75 ng/mL. The within-run precision of the method, expressed as relative std. deviation, ranged 2.1-8.1%. The accuracy, expressed as relative error, ranged from -3.5 to 4.0%. For the main metabolite, the O-demethylated product, the method was linear over the range 7.5-2400 ng/mL, and the limit of quantitation in plasma was 7.5 ng/mL. The within-run precision ranged 2.1-11.0% and the accuracy from -5.3 to 1.1%. Another metabolite, the N-(demethoxyphenylamido) analog, was also detected in plasma. The method was used to follow the time course of BN-50727 and its metabolites in human plasma after administration of single and multiple doses.

IT **132418-35-0**, BN 50727
 RL: ANT (Analyte); ANST (Analytical study)
 (detn. of platelet-activating factor inhibitor BN-50727 and its metabolites in human plasma by HPLC)
 RN 132418-35-0 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



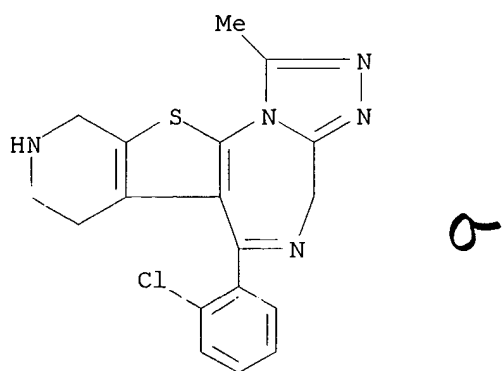
IT **114800-58-7 165898-01-1**
 RL: ANT (Analyte); MFM (Metabolic formation); ANST (Analytical study);
 BIOL (Biological study); FORM (Formation, nonpreparative)
 (detn. of platelet-activating factor inhibitor BN-50727 and its

09/701,893

metabolites in human plasma by HPLC)

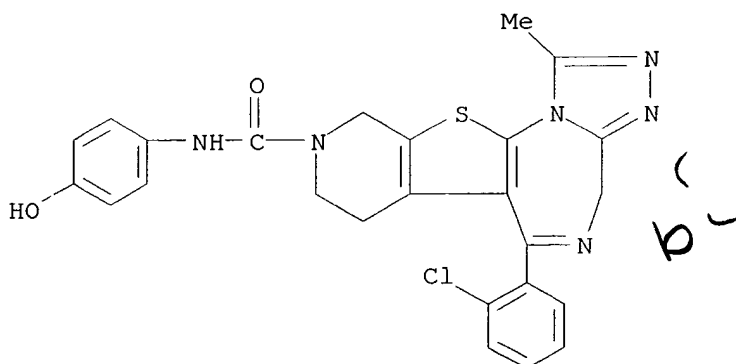
RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



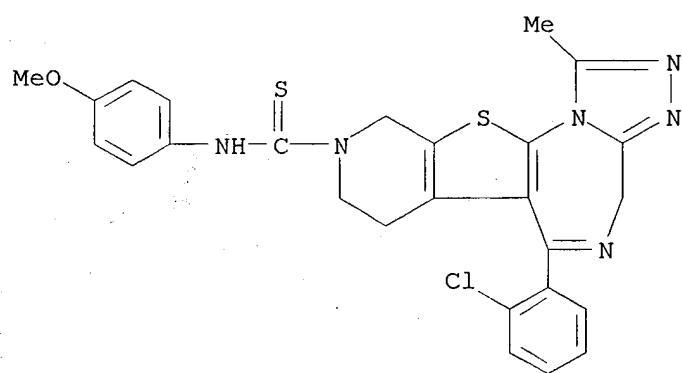
RN 165898-01-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-1-
methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 31 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1995:622062 CAPLUS
DN 123:580
TI Effects of platelet-activating factor antagonists WEB 2086 and BN 50730 on digoxin-induced arrhythmias
AU Cakici, Iclal; Mataraci, Neval; Ersoy, Sibel; Tunctan, Bahar; Abacioglu, Nurettin; Kanzik, Ilker
CS Dep. Pharmacology, Gazi Univ., Ankara, 06330, Turk.
SO Pharmacol. Toxicol. (Copenhagen) (1995), 76(6), 343-7
CODEN: PHTOEH; ISSN: 0901-9928
DT Journal
LA English
AB Effects of platelet-activating receptor antagonists WEB 2086 (1.0-30.0 mg.cntdot.kg-1 i.v.) and BN 50730 (10.0 mg.cntdot.kg-1 i.v.) alone or in combination with CGS 8515 (a specific 5-lipoxygenase inhibitor, 0.3 mg.cntdot.kg-1 i.v.) and Dazmegrel (a thromboxane synthase inhibitor, 1.0 mg.cntdot.kg-1.cntdot.hr-1 i.v. infusion) on digoxin-induced arrhythmias were investigated in anesthetized guinea-pigs. ECG, mean arterial blood pressure, heart rate and arrhythmias were recorded, starting 30 min. before digoxin administration and continuing for 60 min. afterwards. WEB 2086 (10.0 mg.cntdot.kg-1 i.v.) reduced the mortality rate and arrhythmia score significantly compared to the control values. However, in combination with CGS 8515, it did not affect the mortality rate. BN 50730 (10.0 mg.cntdot.kg-1) reduced the incidence of ventricular fibrillation and also arrhythmia score. BN 50730 in combination with Dazmegrel reduced the arrhythmia score, incidence of ventricular fibrillation and mortality rate significantly, compared to control values. Digoxin-induced acute rise in mean arterial blood pressure was not affected by any of drug treatment except WEB 2086 (10.0 mg.cntdot.kg-1) in combination with CGS 8515. Heart rate values did not differ between groups. However, pressure-rate index was reduced by WEB 2086 alone or in combination with CGS 8515. Results showed that although two different platelet-activating factor antagonists have different effects on the incidence of ventricular fibrillation and mortality, they improved the digoxin-induced arrhythmias when they were used either sep. or in combination with CGS 8515 or Dazmegrel, implicating that platelet-activating factor has a role on digoxin-induced arrhythmias.
IT **132579-32-9**, BN 50730
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(WEB 2086 and BN 50730 effects on digoxin-induced arrhythmias)
RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 32 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:467965 CAPLUS

DN 122:281833

TI Mechanisms of the platelet aggregation induced by activated neutrophils and inhibitory effect of specific PAF receptor antagonists

AU Nguyen, Philippe; Petitfrere, Emmanuelle; Potron, Gerard

CS Laboratoire Central Hematologie, CHU Robert-Debre, Reims, 51092, Fr.

SO Thromb. Res. (1995), 78(1), 33-42

CODEN: THBRAA; ISSN: 0049-3848

DT Journal

LA English

AB The supernatant of polymorphonuclear neutrophils after their activation by opsonized zymosan induces the aggregation of washed platelets in human. It potentiates platelet aggregation induced by agonists in platelet rich plasma as well as in whole blood. This activation involves the phosphoinositide metab. Specific PAF receptor antagonist ginkgolides (BN 50726, BN 52021, BN 54068, BN 54062, BN 50730, BN 50749, BN 50744) and benzodiazepine Web2086 antagonize this neutrophil-induced platelet aggregation. BN 50730, BN 50749, and Web2086 can fully inhibit this aggregation at the final concn. of 10^{-6} M. Preincubation of platelets with synthetic PAF also inhibits this activation through a desensitization of the receptor. These data suggest the major involvement in our model of PAF acether in the platelet-neutrophil interactions.

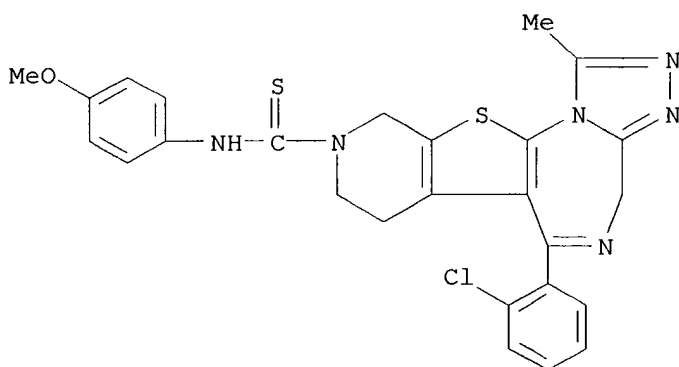
IT 132579-32-9, BN 50730

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

(mechanisms of platelet aggregation induced by activated neutrophils,
and inhibitory effect of specific PAF receptor antagonists)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 33 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:453270 CAPLUS

DN 122:281705

TI Treatment of carrageenan induced arthritis by the platelet activating factor antagonist BN 50730

AU Hilliquin, P; Natour, J; Aissa, J; Guinot, P; Laoussadi, S; Benveniste, J; Menkes, C J; Arnoux, B

CS Service de Rhumatologie A, Hopital Cochin, Paris, Fr.

SO Ann. Rheum. Dis. (1995), 54(2), 140-3

CODEN: ARDIAO; ISSN: 0003-4967

DT Journal

LA English

AB The authors evaluated the role of platelet activating factor (PAF) in the early stage of arthritis. Arthritis was induced in rabbits by weekly intra-articular injections of carrageenan. A PAF receptor antagonist, BN 50730, was used as a preventive or curative agent. BN 50730 was able partially to prevent the development of arthritis, and was also active on established arthritis. The joint arthritis scores of BN treated animals were significantly lower than those of the non-treated animals. The blood concns. of PAF, PAF bound to lipoproteins (lipo-PAF), and its precursor, lyso-PAF, were not correlated with clin. variations. The present data demonstrate a therapeutic action of a PAF antagonist in exptl. arthritis and suggest a crit. role for PAF during the early stage of arthritis.

IT 132579-32-9, BN 50730

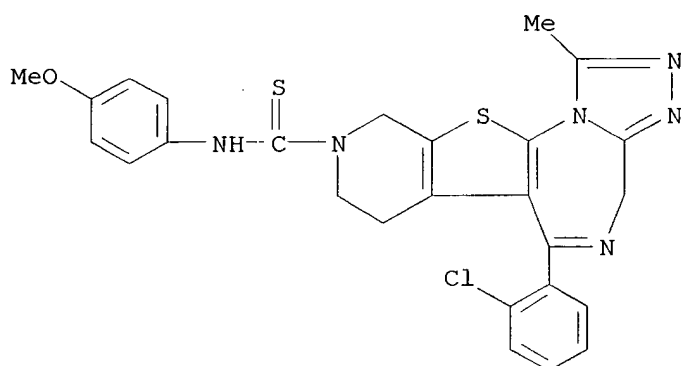
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of carrageenan-induced arthritis with the platelet activating factor antagonist BN 50730)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 34 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:299925 CAPLUS

DN 122:81418

TI Preparation of N-[(quinolylmethoxy)benzoyl]pyridothienotriazolodiazepines and analogs as PAF antagonists and/or 5-lipoxygenase inhibitors

IN Carceller, Elena; Recasens, Nuria; Almansa, Carmen; Bartroli, Javier

PA J. Uriach y Cia. S.A., Spain

SO Eur. Pat. Appl., 15 pp.

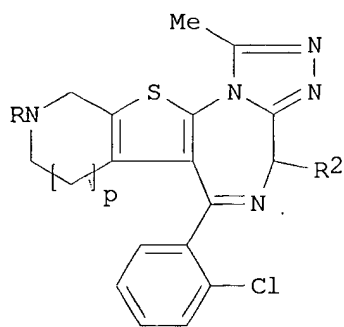
CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 624588	A1	19941117	EP 1994-107134	19940506
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	ES 2061406	A1	19941201	ES 1993-982	19930507
	ES 2061406	B1	19950601		
	CA 2123057	AA	19941108	CA 1994-2123057	19940506
	JP 07002868	A2	19950106	JP 1994-119520	19940509
PRAI	ES 1993-982		19930507		
OS	MARPAT 122:81418				
GI					



I

AB Title compds. [I; R = R₁CH₂OC₆H₄(CH₂)_nCO; R₁ = (chloro- or fluoro-) 2-quinolyl; R₂ = H, alkyl; n, p = 0 or 1] were prepd. Thus, 3-(R₁CH₂O)C₆H₄CO₂H (R₁ = 2-quinolyl) (prepn. given) was condensed with I (R = H, R₁ unchanged) to give I [R = 3-(R₁CH₂O)C₆H₄CO] which gave 72% inhibition of Ca ionophore A23187-induced LTB₄ prodn. by HL-60 cell in vitro.

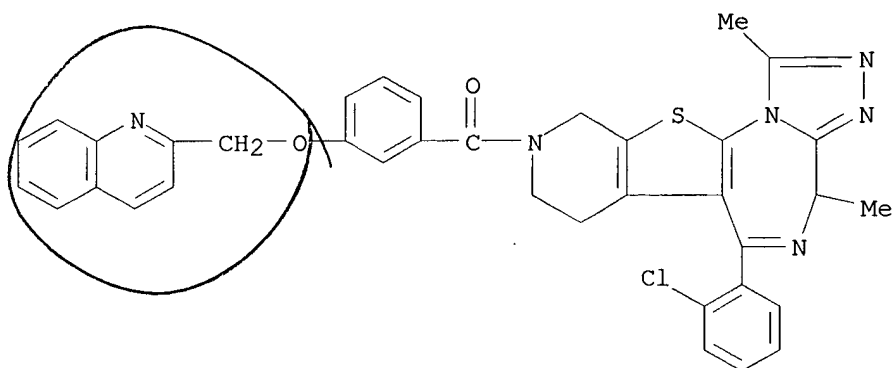
IT **160288-34-6P 160288-35-7P 160288-36-8P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-[(quinolylmethoxy)benzoyl]pyridothienotriazolodiazepines and analogs as PAF antagonists and/or 5-lipoxygenase inhibitors)

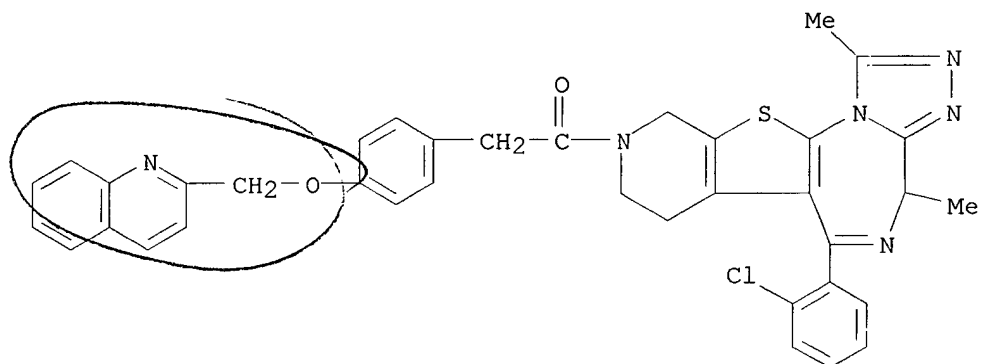
RN 160288-34-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[3-(2-quinolylmethoxy)benzoyl]- (9CI) (CA INDEX NAME)



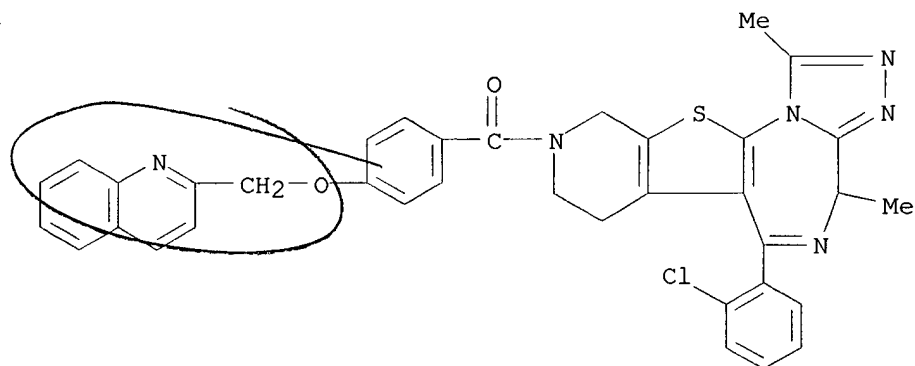
RN 160288-35-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[[4-(2-
quinolinylmethoxy)phenyl]acetyl]- (9CI) (CA INDEX NAME)



RN 160288-36-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[[4-(2-
quinolinylmethoxy)benzoyl]- (9CI) (CA INDEX NAME)



IT 130311-75-0

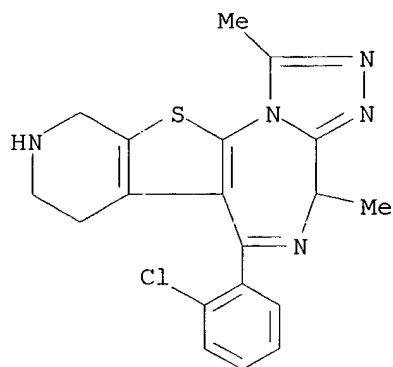
09/701,893

RL: RCT (Reactant)

(prepn. of N-[(quinolylmethoxy)benzoyl]pyridothienotriazolodiazepines and analogs as PAF antagonists and/or 5-lipoxygenase inhibitors)

RN 130311-75-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX
NAME)



○

L23 ANSWER 35 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1995:288848 CAPLUS

DN 122:71670

TI Protective effect of a PAF antagonist and of calcium antagonists on the exacerbation caused by PAF of anoxia-induced myocardial damage

AU Yin, Tao; Guo, Zhaogui

CS Research Section of Pharmacology, Hunan Med. Univ., Changsha, Peop. Rep. China

SO Hunan Yike Daxue Xuebao (1994), 19(4), 283-6

CODEN: HYXBET; ISSN: 1000-5625

DT Journal

LA Chinese

AB The effect of platelet-activating factor (PAF) during acute anoxia of myocardial myocytes cultured from neonatal rats was studied. Lactate dehydrogenase (LDH) in the culture medium was detd. as an index of cell damage. PAF concn.-dependently increased LDH release by anoxic myocytes but had no effect on that by normoxic myocytes. The PAF antagonist BN50730 and the Ca²⁺ antagonists verapamil and bepridil decreased LDH release by PAF-treated anoxic myocytes. It is suggested that the PAF antagonist and the Ca²⁺ antagonists alleviated the cellular damage induced by PAF.

IT 132579-32-9, BN 50730

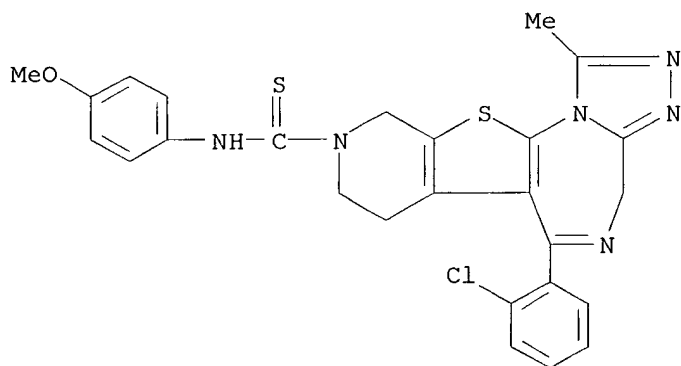
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(protection by platelet-activating factor antagonist and calcium antagonists against heart damage from platelet-activating factor and anoxia)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 36 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:692452 CAPLUS

DN 121:292452

TI Long-lasting inhibitory activity of the hetrazepinic BN 50730 on exudation and cellular alterations evoked by PAF and LPS

AU Pires, Ana L. A.; Silva, Patricia M. R.; Pasquale, Claudia; Castro-Faria-Neto, Hugo C.; Bozza, Patricia T.; Cordeiro, Renato S. B.; Rae, Giles A.; Braquet, Pierre; Lagente, Vincent; Martins, Marco A.

CS Dep. de Fisiologia e Farmacodinamica, Instituto Oswaldo Cruz/FIOCRUZ, Rio de Janeiro, 21045-900, Brazil

SO Br. J. Pharmacol. (1994), 113(3), 994-1000

CODEN: BJPCBM; ISSN: 0007-1188

DT Journal

LA English

AB Inhibitory effects of the hetrazepinic deriv. BN 50730 on the rat pleural inflammatory response, triggered by PAF or lipopolysaccharides (LPS), were examd. The type of pharmacol. blockade exerted by this antagonist in in vitro assays of eosinophil chemotaxis and platelet aggregation were also investigated. Intrathoracic injection of PAF (1 .mu.g per cavity) caused a 4 fold increase in the extravasated protein within 15 min and led to a marked eosinophil accumulation 24 h post-challenge. BN 50730 (0.5-10 .mu.g per cavity) inhibited exudation by PAF dose-dependently without modifying the response induced by histamine, bradykinin or 5-hydroxytryptamine (5-HT). The kinetics of the inhibitory effect on exudation revealed that the actions of WEB 2086 and BN 52021 (10 .mu.g per cavity) were over within 2 and 4 h resp., whereas BN 50730 (10 .mu.g per cavity) retained 80% of its inhibitory activity for 4 days. Oral treatment of BN 50730 (10-20 mg kg⁻¹, 1 h beforehand) suppressed the leukocyte accumulation and late eosinophilia obsd. 6 and 24 h after PAF resp., but did not modify the eosinophilia induced by leukotriene B4 (LTB4) or bradykinin. BN 50730 also failed to reduce the eosinophil accumulation induced by LPS but drastically inhibited the neutrophil influx. The pre-incubation of rat peritoneal eosinophils for 10 min with BN 50730 (30 nM-1 .mu.M) dose-dependently inhibited the chemotaxis induced by PAF (0.1 .mu.M) in vitro. The IC50 values for BN 52021, WEB 2086 and BN 50730 in this system were 5, 5 and 0.05 .mu.M resp. In sep. assays, rat peritoneal eosinophils and rabbit washed platelets were preincubated with BN 50730 or WEB 2086 (1 .mu.M) then subjected to a series of at least two consecutive washings in order to remove the antagonist from the receptor environment. Under such conditions, only the cells pretreated with WEB 2086 recovered the sensitivity to the lipid. We conclude that BN 50730 is a potent, specific and long-acting PAF antagonist and its effect seems to result from a high affinity and non-competitive interaction of the drug with the PAF receptor.

IT **132579-32-9**, BN 50730

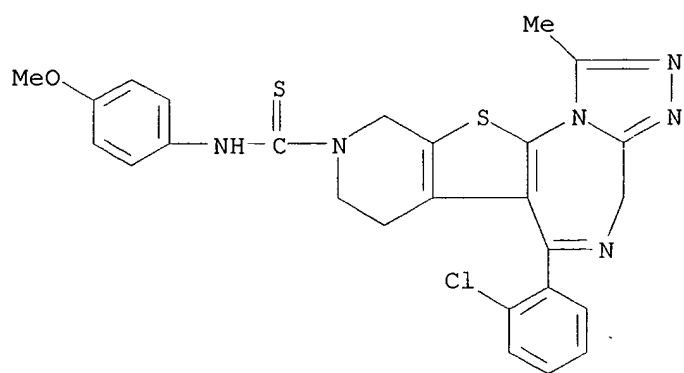
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(by hetrazepinic BN 50730 long-lasting inhibition of exudation and cellular alterations evoked by PAF and LPS)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 37 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:672066 CAPLUS

DN 121:272066

TI Effect of the hetrazepinic BN 50730 on the pleural exudatory and cellular responses triggered by PAF in rats

AU Martins, M. A.; Pires, A. L. A.; Silva, P. M. R.; Pasquale, C. P.; Lagente, V.; Braquet, P.; Cordeiro, R. S. B.

CS Dep. Fis. Farmacodinamica, Fundacao Oswaldo Cruz, Rio de Janeiro, 21045-900, Brazil

SO J. Lipid Mediators Cell Signalling (1994), 10(1-2), 133-4
CODEN: JLMSEO; ISSN: 0929-7855

DT Journal

LA English

AB BN 50730 is a potent, specific and long-lasting PAF antagonist on pleurisy and eosinophil chemotaxis induced by PAF. BN 50730, intrathoracic administration (2.5-10 .mu.g/cavity) in rats, caused a dose-dependent inhibition of protein exudation and oral pretreatment with it, before PAF challenge, suppressed the 6 h neutrophilia and late eosinophilia triggered by PAF.

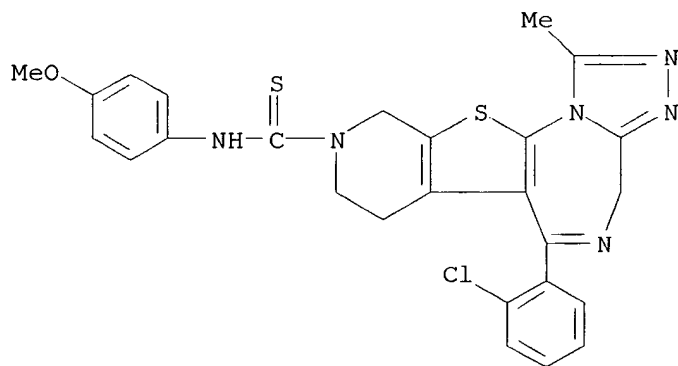
IT 132579-32-9, Bn 50730

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(BN 50730 effect on pleurisy and eosinophil chemotaxis induced by PAF)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

123 ANSWER 38 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:671824 CAPLUS

DN 121:271824

TI Effect of PAF-antagonists on aeroallergen-induced bronchial eosinophilia in guinea pigs: a therapeutic approach

AU Chand, N.; Harrison, J. E.; Sofia, R. D.

CS Wallace Lab., Div. Carter-Wallace, Inc., Cranbury, NJ, 08512, USA

SO Res. Commun. Mol. Pathol. Pharmacol. (1994), 86(1), 75-82

CODEN: RCMPE6

DT Journal

LA English

AB Aeroallergen-induced eosinophilia in actively sensitized guinea pigs was used as a marker of bronchial inflammation in this study. Drugs were administered p.o. therapeutically, i.e., four hours after aeroallergen challenge. Allergic bronchial eosinophilia in guinea pigs was sensitive to dexamethasone. Thus, the therapeutic approach appears to be reliable, and sensitive for the evaluation and selection of potential bronchial anti-inflammatory compds. PAF-antagonists (WEB-2086, WEB-2170, and E-6123) and a 5-lipoxygenase inhibitor (E-6080) did not influence allergen-induced eosinophil infiltration in the bronchoalveolar lavage fluid. These observations seem to suggest that therapeutic administration of PAF antagonists and leukotriene synthesis inhibitors exert little or no inhibitory effect on the progression of late-phase allergic bronchial inflammation in this model.

IT 131614-02-3, E-6123

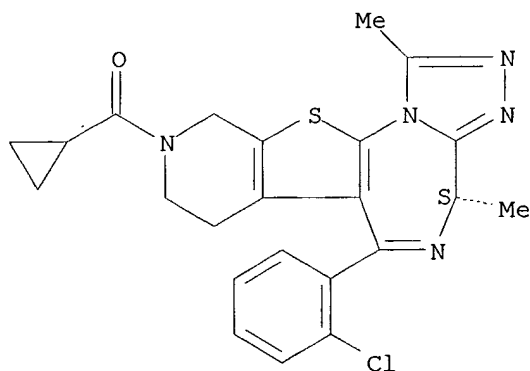
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of PAF-antagonists on aeroallergen-induced bronchial eosinophilia)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 39 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:671735 CAPLUS

DN 121:271735

TI Effect of BN 50730, a specific PAF antagonist, on PAF-induced platelet aggregation and skin responses in healthy human volunteers

AU Duchier, Jacques; Auriche, Caroline; Guinot, Philippe

CS Hopital de St Cloud, Paris, Fr.

SO Drug Invest. (1994), 8(2), 95-103

CODEN: DRUIEA; ISSN: 0114-2402

DT Journal

LA English

AB The effect of the oral administration of BN 50730, a specific synthetic platelet-activating factor (PAF) receptor antagonist, on 2 recognized PAF-induced reactions (ex vivo platelet aggregation and immediate cutaneous responses), was assessed through 3 double-blind placebo-controlled studies in healthy, non-allergic male volunteers. Platelet aggregation showed a peak level of inhibition 4 h following the single administration of either a 10, 20 or 40mg dose. A dose-response relationship was obsd. regarding the duration of the effect; while lasting <12 h for the 10 mg dose, inhibition was still evident 16 h after administration of the 40 mg dose. Wheal and flare reactions to intradermal PAF (400 ng) were significantly inhibited following single dose administration of either 10, 20 or 40 mg of BN 50730. The 40-mg dose inhibited the flare reaction by more than 90% at 8 h post-treatment. Treatment with either 20 or 40-mg of BN 50730 twice daily for 7 days resulted in a redn. in the cutaneous responses to PAF after the last dose by at least 80% compared with placebo in both treatment groups, the 2 doses being almost equally effective. BN 50730 is a potent PAF antagonist and provide interesting information for testing the product at 40 or 80 mg dose levels in twice-daily phase II clin. studies.

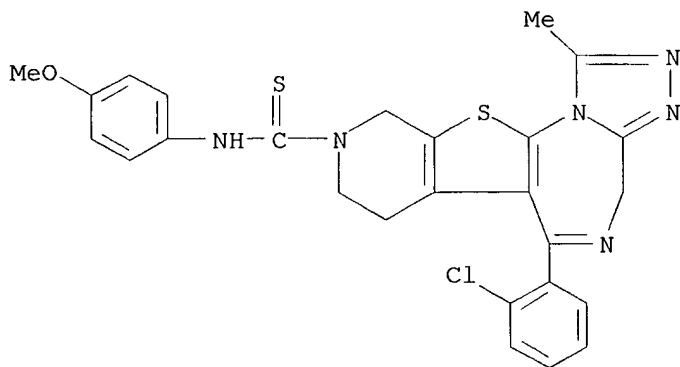
IT 132579-32-9, BN 50730

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

(BN 50730 effect on blood platelet aggregation and skin responses in humans)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 40 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:653466 CAPLUS

DN 121:253466

TI The platelet activating factor antagonist, BN 50730, protects against the development of experimental autoimmune encephalomyelitis

AU Spinnewyn, B.; Blavet, N.; Pirotzky, E.; Braquet, P.

CS Henri Beaufour Inst., Les Ulis, 91952, Fr.

SO J. Lipid Mediators Cell Signalling (1994), 10(1-2), 135-7

CODEN: JLMSEO; ISSN: 0929-7855

DT Journal

LA English

AB The authors studied whether the level of peripheral type benzodiazepine binding sites (PTBBS) in spinal cord homogenates (contg. T cells and macrophages) could be modified after induction of exptl. allergic encephalomyelitis (EAE) in the Lewis rat. In addn., the effect of the specific PAF receptor antagonist BN 50730 on EAE was studied. In the spinal cord homogenate a single class of PTBBS binding sites was found, and EAE induced an increase in the nos. of PTBBS obsd. BN 50730 at 3 and 10 mg/kg prevented the appearance of paralysis, and at 3 mg/kg decreased the no. of PTBBS as compared to the EAE controls. The clin. signs of EAE and increase in PTBBS in spinal cord in EAE was attenuated by BN 50730 at 3 mg/kg.

IT 132579-32-9, Bn 50730

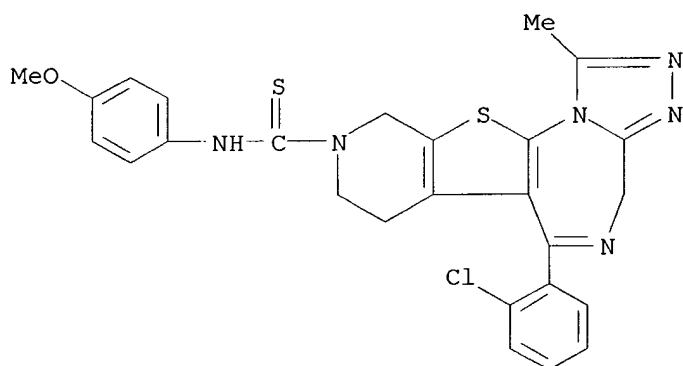
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(platelet activating factor antagonist BN 50730 protects against autoimmune encephalomyelitis and increase of peripheral type benzodiazepine binding sites)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 41 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:621776 CAPLUS

DN 121:221776

TI Effect of antagonists of platelet-activating factor receptors on memory of inhibitory avoidance in rats

AU Jerusalinsky, Diana; Fin, Cyntia; Quillfeldt, Jorge A.; Ferreira, Maria Beatriz C.; Schmitz, Paulo K.; Silva, Ricardo C. Da; Walz, Roger; Bazan, Nicolas G.; Medina, Jorge H.; et al.

CS Departamento de Bioquimica, Centro de Memoria, Porto Alegre, 90046-900, Brazil

SO Behav. Neural Biol. (1994), 62(1), 1-3

CODEN: BNBIDY; ISSN: 0163-1047

DT Journal

LA English

AB Platelet-activating factor (PAF) is present in the brain. It enhances glutamate release and long-term potentiation (LTP) through an action on synaptic membrane receptors sensitive to the antagonist, BN 52021, and has been proposed as a retrograde messenger in the genesis of LTP. In addn., PAF has other, metabolic actions mediated by microsomal receptors sensitive to the antagonist, BN 50730. We investigated the effect on memory of the pre- or post-training infusion of BN 52021 or BN 50730 into the hippocampus and that of BN 52021 in the amygdala and the entorhinal cortex. Male Wistar rats were implanted bilaterally with cannulae aimed at these brain regions. After recovery from surgery, the animals were trained in step-down inhibitory avoidance using a 0.5-mA foot shock and tested for retention 24 h later. BN 52021 (0.5 .mu.g/side) was amnesic when given into the hippocampus or the amygdala either before or immediately after training but not 30 or 100 min later. BN 52021 was also amnesic when given into the entorhinal cortex 100 but not 0 or 300 min after training. Intrahippocampally administered BN 50730 had no effect on memory. The findings are compatible with the suggestion from previous findings that memory of this task depends on the generation of LTP at the time of training in hippocampus and amygdala and, 90-180 min later, in the entorhinal cortex.

IT 132579-32-9, BN 50730

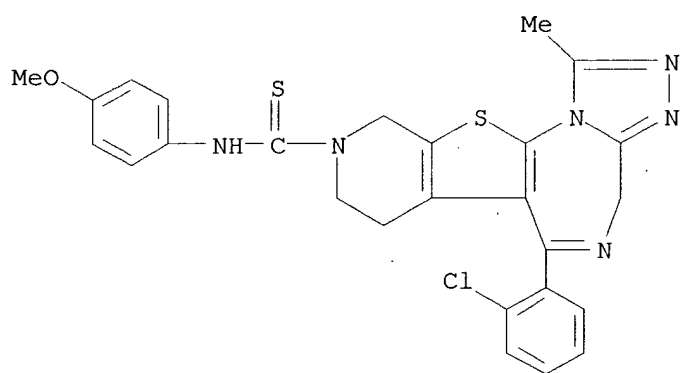
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(platelet-activating factor antagonists effect on memory of inhibitory avoidance)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 42 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:620893 CAPLUS

DN 121:220893

TI Determination of the platelet activating factor antagonist
6-(2-chlorophenyl)-9-[(4-methoxyphenyl)thiocarbamoyl]-1-methyl-7,8,9,10-tetrahydro-4H-pyrido[4',3'-4,5]-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine in human plasma by liquid chromatography-thermospray mass spectrometry

AU Celma, C.

CS Mass Spectrometry Department, S.A. LASA Laboratorios, Ctra. Laurea Miro 395, Sant Feliu de Llobregat, Barcelona, E-08980, Spain

SO J. Chromatogr., B: Biomed. Appl. (1994), 657(1), 214-18
CODEN: JCBBEF

DT Journal

LA English

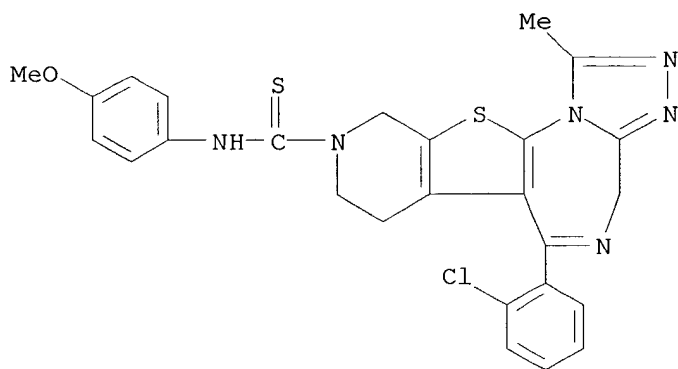
AB A sensitive and specific method for the detn. of the platelet activating factor (PAF) antagonist 6-(2-chlorophenyl)-9-[(4-methoxyphenyl)thiocarbamoyl]-1-methyl-7,8,9,10-tetrahydro-4H-pyrido[4',3'-4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (I) in human plasma is described. The target mol. was analyzed by high-performance liq. chromatog. (HPLC) coupled to mass spectrometry (MS) after extn. by ion-exchange chromatog. HPLC was carried out using a C18 column and the coupling to the MS was done by a thermospray (TSP) interface working in the direct ion-evapn. ionization mode in presence of 0.1 M ammonium acetate. Selected-ion monitoring (SIM) was carried out for the ion m/z 370 and its [M+2]⁺ isotopic peak. Evaluation of the intensity matching of such ions has been used in the validation results. The method gives good accuracy and precision over the concn. range 1-200 ng I/mL human plasma.

IT 132579-32-9

RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood of humans by liq. chromatog.-thermospray mass spectrometry)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 43 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:594816 CAPLUS

DN 121:194816

TI Quantitative measurement of BN50727 in human plasma and urine by combined liquid chromatography/negative ion chemical ionization mass spectrometry using a particle beam interface

AU Girault, J.; Malgouyat, J. M.; Lecomte, G.; Longueville, D.; Istin, B.; Fourtillan, J. B.

CS CEMAF Res. Centre, Poitiers, 86000, Fr.

SO Biol. Mass Spectrom. (1994), 23(9), 581-9

CODEN: BIMSEH; ISSN: 1052-9306

DT Journal

LA English

AB A new sensitive assay has been developed for the quant. measurement of BN50727 at the picomole level in human plasma and urine. The drug and the internal std. (BN50788) were measured by combined liq. chromatog./neg. ion chem. ionization mass spectrometry with methane as the reagent gas. A simple solid-liq. extn. procedure was used to isolate BN50727 from the complex biol. matrixes. The mass spectrometer was tuned to monitor the intense and stable ion at m/z 333 which was generated in the ion source by a dissociative capture process. This assay was performed with 1 mL of plasma or 0.1 mL of urine and the quantification limit of the method was statistically calcd. as 1 ng mL⁻¹. The very low relative std. deviations and mean percentages of error calcd. during the different within-day or between-day repeatability assays have clearly demonstrated the ruggedness of the technique for the routine detn. of BN50727 in biol. fluids. Some preliminary results on the pharmacokinetics of the drug are presented to illustrate the applicability of this powerful liq. chromatog./mass spectrometric method.

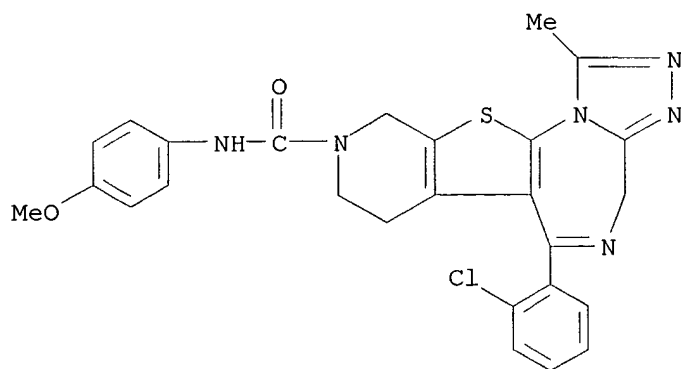
IT 132418-35-0, BN50727

RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(quant. measurement of BN50727 in human plasma and urine by combined liq. chromatog. neg. ion chem. ionization mass spectrometry using particle beam interface and pharmacokinetics)

RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 44 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:594811 CAPLUS

DN 121:194811

TI Simultaneous quantitative measurement of a new platelet activating factor antagonist (BN 50730) and its two main metabolites in human plasma and urine by LC-MS

AU Girault, J.; Longueville, D.; Malgouyat, J. M.; Istin, B.; Lecomte, G.; Fourtillan, J. B.

CS CEMAF Research Centre, Poitiers, 86000, Fr.

SO Chromatographia (1994), 39(3-4), 228-38

CODEN: CHRGB7; ISSN: 0009-5893

DT Journal

LA English

AB A simple and sensitive assay has been developed for the quant. measurement of a new platelet activating factor antagonist (BN 50730), and its two main metabolites (BN 50727 and BN 50922), at the picomole level in human plasma and urine. The three compds. of interest and the internal std. (BN 50765) were measured by combined LC-neg. chem. ionization MS. A simple solid-liq. extn. procedure was used to isolate the parent drug and the two metabolites. The MS was tuned to monitor the intense ion m/z 333 generated in the ion source by a dissociative capture process. The assay was on 1 mL plasma or 0.1 mL urine and the quantitation limit was calcd. as 1 ng.cntdot.mL⁻¹. The very low relative std. deviations and mean percentages of error calcd. for within-day or between-day repeatability assays demonstrate the ruggedness of the technique for routine detn. in biol. fluids. Some preliminary results on the pharmacokinetics of the parent drug and its two main metabolites illustrate the applicability of this method.

IT 132418-35-0, BN 50727 132579-32-9, BN 50730

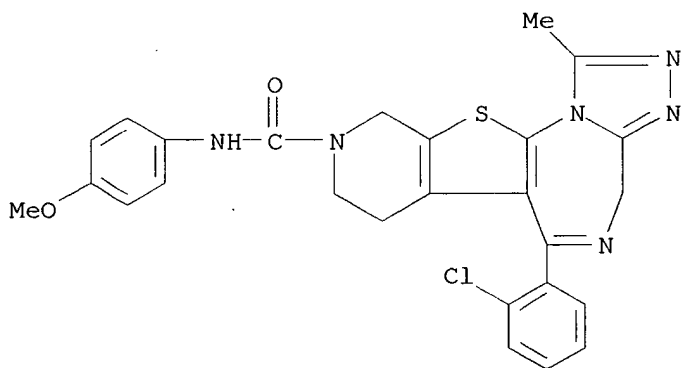
153339-88-9, BN 50922

RL: ANT (Analyte); ANST (Analytical study)

(LC-MS detn. of BN 50730 and metabolites in human plasma and urine)

RN 132418-35-0 CAPLUS

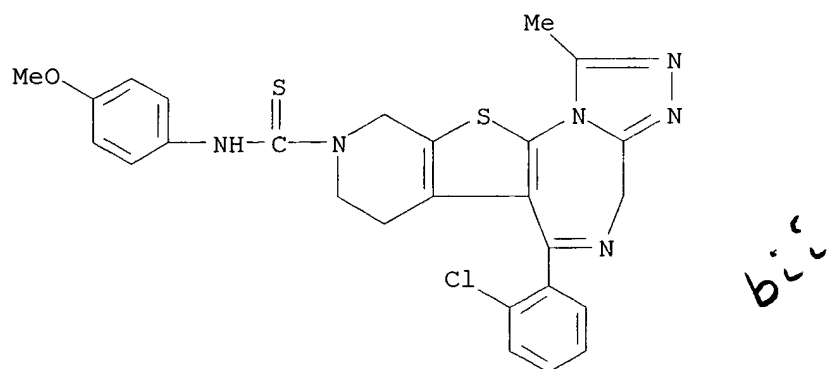
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



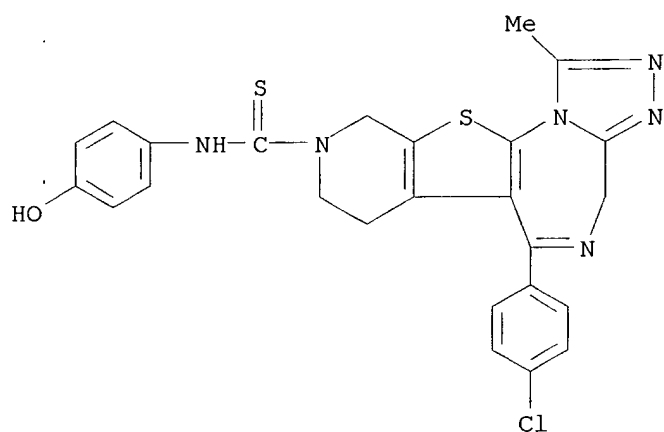
RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 153339-88-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-
1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 45 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:594796 CAPLUS

DN 121:194796

TI Quantitative measurement of a new synthetic hetrazepine derivative, BN50730, in human plasma and urine by combined liquid chromatography-negative chemical ionization mass spectrometry using a particle beam interface

AU Girault, J.; Malgouyat, J. M.; Longueville, D.; Lecomte, G.; Revaud, M.; Fourtillan, J. B.

CS Cemaf Research Centre, 6 avenue Mozart, Poitiers, 86000, Fr.

SO J. Chromatogr., B: Biomed. Appl. (1994), 658(2), 289-301

CODEN: JCBBEF

DT Journal

LA English

AB A new simple and sensitive assay has been developed for the quant. measurement of BN50730 at the picomole level in human plasma and urine. The drug and the internal std. (BN50765) were measured by combined liq. chromatog.-neg. chem. ionization mass spectrometry with methane as the reagent gas. A simple solid-liq. extn. procedure was used to isolate BN50730 from complex biol. matrixes. Mild operating conditions were required to assay the parent drug with a particle beam interface from Hewlett-Packard. The mass spectrometer was tuned to monitor the intense ion m/z 333, which was generated in the ion source by a dissociative capture process. This assay was performed with 1 mL of plasma or 0.1 mL of urine, and the quantification limit of the method was statistically calcd. as 1 ng mL⁻¹. The very low relative std. deviation and mean percentage of error calcd. during the different within-day or between-day repeatability assays clearly demonstrate the ruggedness of the technique for the routine detn. of BN50730 in the biol. fluids. Some preliminary results on the pharmacokinetics of the drug are presented to illustrate the applicability of this new powerful LC-MS method.

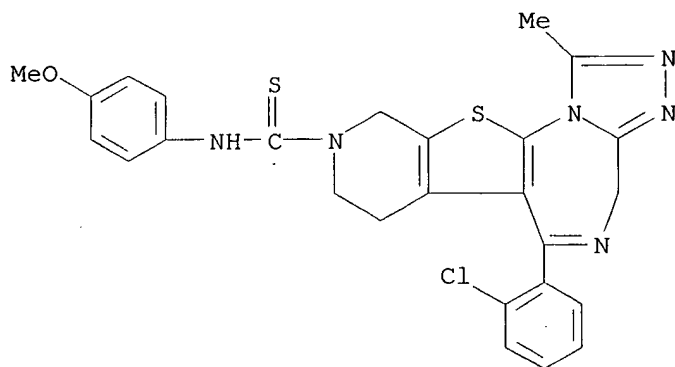
IT 132579-32-9, BN50730

RL: ANT (Analyte); ANST (Analytical study)

(detn. of hetrazepine deriv. BN50730 in human plasma and urine by combined liq. chromatog.-neg. chem. ionization mass spectrometry using a particle beam interface)

RN 132579-32-9 CAPLUS

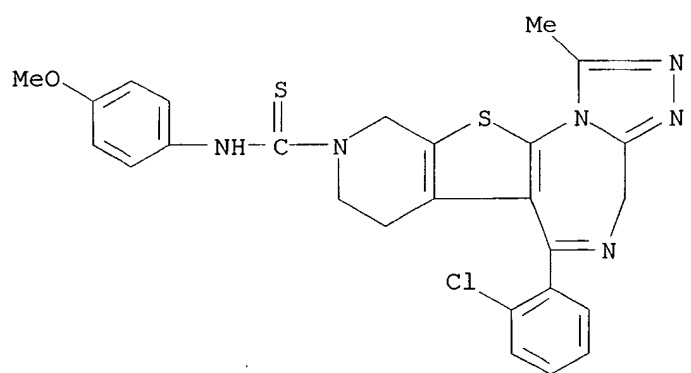
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



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L23 ANSWER 46 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1994:475176 CAPLUS
DN 121:75176
TI Platelet-activating factor and retinoic acid synergistically activate the inducible prostaglandin synthase gene
AU Bazan, Nicolas G.; Fletcher, Bradley S.; Herschman, Harvey P.; Mukherjee, Pranab K.
CS Louisiana State Univ. Neurosci., Louisiana State Univ. Med. Cent., New Orleans, LA, 70112, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(12), 5252-6
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Platelet-activating factor (PAF), a potent lipid mediator generated in cell injury and in the inflammatory and immune responses, promotes transcriptional activation of several primary responses genes. TIS10/PGS-2 is a primary response gene encoding the inducible form of prostaglandin synthase. The inductive effects of PAF and retinoic acid (RA), alone and in combination, were studied with the regulatory region of TIS10/PGS-2 transfected into an exponentially growing glioblastoma-neuroblastoma NG108-15 hybrid in the human SH-SY5Y neuroblastoma or in the NIH 3T3 cell. RA alone exhibited only a small inductive effect. However, in the presence of RA (100 nM), a PAF-dependent (1-50 nM) synergistic of RA (100 nM), a PAF-dependent (1-50 nM) synergistic activation of luciferase reporter constructs driven by regulatory regions of the TIS10/PGS-2 gene was found. The hexazepine BN-50730, an antagonist selective for intracellular PAF binding sites, inhibited PAF and RA induction of luciferase from the TIS10/PGS-2 promoter. Thus, the intracellular PAF binding site is involved in TIS10/PGS-2 expression. Induction is rapid, suggesting that the combination of PAF and RA activates a preexisting latent transcription factor(s). Deletion studies restrict the major PAF and RA cis-acting response element of the TIS10/PGS-2 gene to a 70-nucleotide sequence as an intracellular inducer of TIS10/PGS-2 expression. The synergistic effect of RA and PAF represents an unusual convergence of nuclear signaling pathways by which, through the modulation of preexisting transcription factors, specific gene expression can be upregulated. PAF-dependent induction of TIS10/PGS-2 expression may play a role in cell injury, differentiation, inflammation, and immune responses.
IT **132579-32-9**, BN-50730
RL: BIOL (Biological study)
(antagonist for intracellular platelet activating factor, retinoic acid and PAF induction of gene PBS-2/TIS10 promoter inhibition by)
RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



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~~L23~~ ANSWER 47 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:400191 CAPLUS

DN 121:191

TI Dual effects of a novel thienodiazepine platelet-activating factor antagonist, on drug-oxidizing enzymes in beagle dog

AU Tanaka, E.; Daling, Z.; Abe, K.; Nakamura, T.; Horie, T.

CS Inst. Community Med., Univ. Tsukuba, Tsukuba, 305, Japan

SO Xenobiotica (1994), 24(4), 293-300

CODEN: XENOBH; ISSN: 0049-8254

DT Journal

LA English

AB The authors have examd. the effects of (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (E-6123), a novel thienodiazepine platelet-activating factor antagonist, on drug-oxidizing capacity in beagle dog, using antipyrine (AP) and trimethadione (TMO) as two model substrates. The plasma half-life ($t_{1/2}$) and area under the curve (AUC) of AP (0.5 mg/kg, i.v. injection) increased in a dose-dependent manner after a single oral dose of E-6123 (0.2, 1 or 10 mg/kg), whereas the total body clearance (Cl) of AP was decreased, and the apparent vol. of distribution (Vd) was unchanged. The pharmacokinetic parameters ($t_{1/2}$, Cl and AUC) of the metab. of TMO (4 mg/kg i.v.) after repeated oral administration of E-6123 (10 mg/kg for 7 days) were not significantly changed in comparison with findings in control dog. The ratio of dimethadione (DMO), being the only TMO metabolite, to TMO in plasma after i.v. administration of TMO in E-6123-treated dog was increased only 5 and 15 min after the final dose, but was not changed at other sampling times (0.5, 1, 2, 4, 6, 8 and 12 h). The content of b5, the activity of p-nitroanisole O-demethylase and benzphetamine N-demethylase were significantly increased, compared with controls, by repeated E-6123 treatment. However, aniline hydroxylase activity was not significantly changed. Content of P 450 2B was significantly increased in E-6123 treated dog, while that of 3A was not. A typical P 450-dependent spectral change was produced by E-6123 in dog microsomes, characterized by a dissocn. const. (K_s) of 230 μ M, compared with 820 μ M for cimetidine. These results suggest that the repeated oral administration of E-6123 has a dual effect (inhibition and induction) on hepatic drug-oxidizing capacity in dog.

IT **131614-02-3**, E-6123

RL: BIOL (Biological study)

(drug-metabolizing enzymes induction and inhibition by)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

X ANSWER 48 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:289318 CAPLUS

DN 120:289318

TI Development of radioimmunoassay for the novel platelet activating factor receptor antagonist, E6123, and its application to pharmacokinetics in laboratory animals

AU Kusano, Kazutomi; Tadano, Kyoichi; Tanaka, Shigeru; Kagei, Yoshiko; Ueda, Masataka; Miyazawa, Shuhei; Abe, Yoshihisa; Ida, Satoshi; Yuzuriha, Teruaki

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SO Biol. Pharm. Bull. (1994), 17(2), 334-9

CODEN: BPBLEO; ISSN: 0918-6158

DT Journal

LA English

AB A direct RIA for the detn. of E6123, a novel antagonist of platelet activating factor (PAF) receptor, was developed to study the pharmacokinetics at low dose. This procedure used [³H]E6123 as the radioligand and an antiserum obtained from rabbits immunized with the hapten covalently bound to bovine serum albumin. M1B, one of the main metabolites of E6123, exhibited cross-reactivity with antisera. But this metabolite had no effect on measurements of E6123, because the amt. of M1B in plasma radioactivity after administration of [¹⁴C]E6123 to dogs and monkeys was low. The sensitivity limit of this assay was 25 pg/mL of plasma when 0.1 mL of plasma was used and the assay showed good accuracy and high precision. The validity of the RIA was demonstrated by comparative anal. of a no. of samples after oral and i.v. administration (1.0 mg/kg) by an HPLC-UV method ($r = 0.972-0.984$, slope = 1.0314-1.2143). The pharmacokinetics of E6123 was studied at a dose of 30 μ g/kg. After i.v. administration, the plasma concn.-time curves in all species fitted a two-compartment model and the terminal half-lives in guinea pigs, dogs and monkeys (both poor and extensive metabolizers) were 4.77, 1.71, 5.34 and 1.07 h, resp. After oral administration, the max. plasma concns. were obtained within 0.83-3.00 h and the half-life for each animal was almost the same as that after i.v. administration. The mean bioavailabilities of E6123 in guinea pigs, dogs and monkeys (poor and extensive metabolizers) were 106.9, 45.7, 59.1 and 22.8%, resp.

IT **131614-02-3**, E6123

RL: ANST (Analytical study)

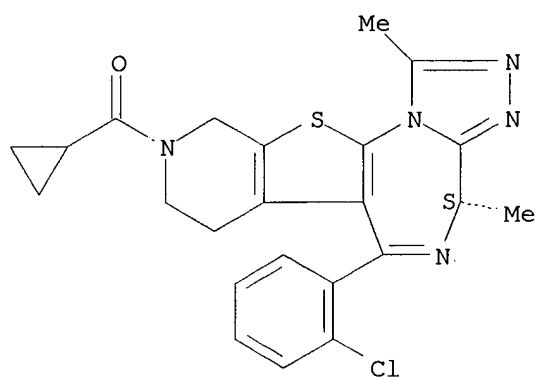
(detn. in blood by RIA and pharmacokinetics of)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

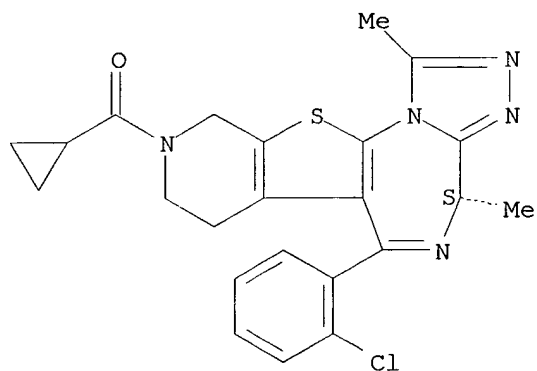
Absolute stereochemistry.

09/701,893



IT **131614-02-3DP**, E6123, serum albumin conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for RIA)
RN 131614-02-3 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



~~123~~ ANSWER 49 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AM~~ 1994:270466 CAPLUS

DN 120:270466

TI Prepn. of diazepines for treatment of osteoporosis

IN Tahara, Tetsuya; Moriwaki, Minoru; Chiba, Kenji; Manabe, Shunichi; Shindo, Masanori; Nakagawa, Takashi; Nakamura, Takeshi

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan; Japan Tobacco, Inc.

SO PCT Int. Appl., 202 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9307129	A1	19930415	WO 1992-JP1325	19921012
	W: CA, HU, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	EP 638560	A1	19950215	EP 1993-906348	19921012
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	US 5593988	A	19970114	US 1994-211572	19940802
	US 5753649	A	19980519	US 1996-706350	19960830
PRAI	JP 1991-327954		19911011		
	WO 1992-JP1325		19921012		
	US 1994-211772		19940802		

OS MARPAT 120:270466

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; Ar = aryl, heteroaryl; X = O, S; Y = H, alkyl, alkenyl, alkynyl, carboxyalkyl, alkoxyalkyl, etc.; or XY = :N=N:CR₆, etc.; R₆ = H, halo, alkyl, alkenyl, etc.; W = imino; R = H, alkyl, haloalkyl, aryl, heteroaryl, aralkyl; R₁ = H, CO₂H, alkoxyalkyl, etc.; Q ring = (un)substituted benzene residue, (un)substituted thiophene residue, etc.] are prepd. Refluxing a mixt. of the aminothiophene deriv. II (R₂ = H) with DL-N-phthaloylphenylalanyl chloride in CHCl₃ gave II (R₂ = N-phthaloylphenylalanyl), which was treated with H₂NNH₂.H₂O in MeOH at room temp. for 4 h and then with concd. HCl at 60.degree. for 3 h to give , after treatment with 5% NaHCO₃, the thienodiazepine III, which was cyclocondensed with H₂NNH₂.H₂O and MeC(OEt)₂ to give the title compd. IV. In a study using bones of mice treated with 45Ca, this at 20 .mu.M decreased Ca resorption by 30.7%.

IT **131614-02-3P**

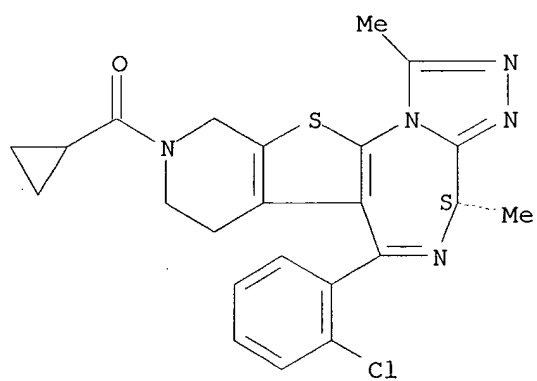
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of osteoporosis)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



L23 ANSWER 50 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:182706 CAPLUS

DN 120:182706

TI Prevention of chloroquine-induced electroretinographic damage by a new platelet-activating factor antagonist, BN 50730

AU Doly, Michel; Cluzel, Jacques; Millerin, Martine; Bonhomme, Brigitte; Braquet, Pierre

CS Lab. Biophys., Fac. Med., Clermont-Ferrand, F-63001, Fr.

SO Ophthalmic Res. (1993), 25(5), 314-18

CODEN: OPRSAQ; ISSN: 0030-3747

DT Journal

LA English

AB Chloroquine retinopathy is a severe toxic retinal impairment which may result in loss of vision by alterations of the retinal pigment epithelium and photoreceptors. Currently, there is no specific treatment for this retinopathy. Platelet-activating factor (PAF) is known to modulate retinal function and is one of the major immunomediators of the retina. In order to test the possible involvement of PAF in chloroquine-induced retinopathy and the effectiveness of PAF antagonists in the prevention of this condition, the authors investigated the effects of BN 50730, a specific PAF antagonist, on the electroretinogram (ERG) of the isolated rat retina exposed to chloroquine. When retinas from normal rats were perfused with chloroquine (10⁻⁶ M), a marked and rapid decrease in b-wave amplitude was obsd. In contrast, chloroquine had no effect on the b-wave of the retina isolated from animals pretreated with the PAF antagonist BN 50730 (30 mg/kg/day, i.p., for 5 days). The results obtained indicate that (i) chloroquine is a toxic drug for retinal function, (ii) PAF plays a key role in the mediation of chloroquine retinopathy and (iii) PAF antagonists may constitute valuable agents for the treatment of this retinal impairment.

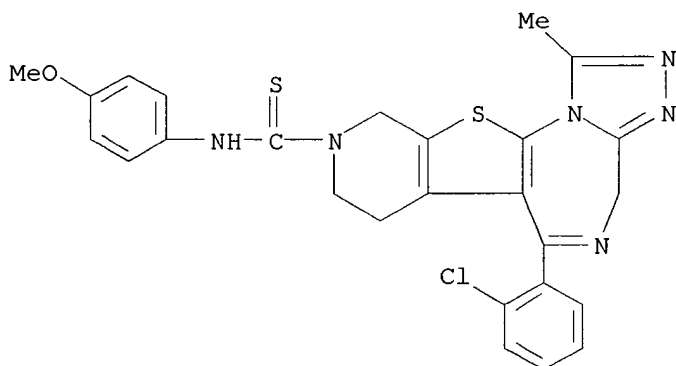
IT 132579-32-9, BN 50730

RL: BIOL (Biological study)

(chloroquine-induced retinopathy prevention by, as platelet-activating factor antagonist)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 51 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:160651 CAPLUS

DN 120:160651

TI Platelet-activating factor is a messenger in the electroconvulsive shock-induced transcriptional activation of c-fos and zif-268 in hippocampus

AU Marcheselli, V. L.; Bazan, N. G.

CS Med. Cent., Louisiana State Univ., New Orleans, LA, 70112, USA

SO J. Neurosci. Res. (1994), 37(1), 54-61

CODEN: JNREDK; ISSN: 0360-4012

DT Journal

LA English

AB Platelet-activating factor (PAF, 1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine), undetectable in resting neural tissue, accumulates in brain during seizures. A betrazepine, BN-50730, is shown here to displace [3H]PAF-specific binding from microsomal, but not from synaptosomal membranes, indicating selectivity for a high affinity intracellular binding site. Rats pretreated with BN-50730 by i.p. or intracerebroventricular injection exhibited an inhibition of the electroconvulsive block (ECS)-induced expression of c-fos and zif-268 in hippocampus. A much more pronounced, dose-dependent inhibition of ECS-induced zif-268 mRNA in hippocampus by intracerebroventricular injection of BN-50730 was obsd. It is concluded that, in the hippocampus, PAF is a mediator of the expression of zif-268 and, to a lesser extent, c-fos through an intracellular specific binding site. Thus, PAF may be a messenger in signal regulated zinc-finger transcription factors, and in other immediate-early genes involved in long-term synaptic plasticity changes.

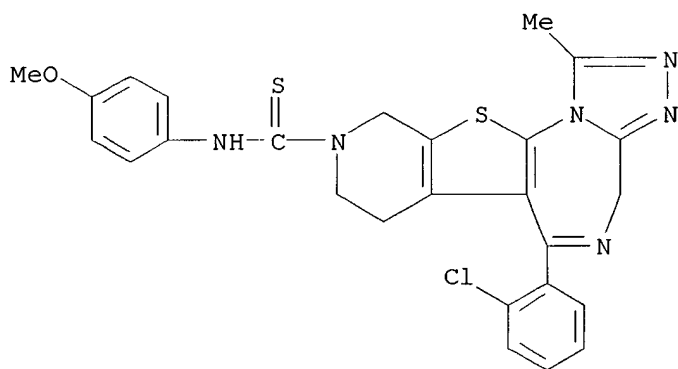
IT 132579-32-9, BN-50730

RL: BIOL (Biological study)

(PAF binding by microsome inhibition by, specificity of)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

L23 ANSWER 52 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:153730 CAPLUS

DN 120:153730

TI Synergistic combinations of PAF antagonists and anticholinergic agents as drugs for treatment of bronchial asthma.

IN Heuer, Hubert

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 13 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4219659	A1	19931223	DE 1992-4219659	19920616
OS	MARPAT 120:153730				

AB Mixts of hetrazepine deriv. PAF antagonists (Markush given) with anticholinergics are synergistic drugs for treatment of bronchial asthma. The effectiveness of a combination of atropine with WEB 2170 was shown on PAF-induced bronchoconstriction, in guinea pigs.

IT ~~128672-07-1D~~, BN 50739, mixts. with anticholinergics

~~131614-02-3D~~, E 6123, mixts. with anticholinergics

~~132418-35-0D~~, BN 50727, mixts. with anticholinergics

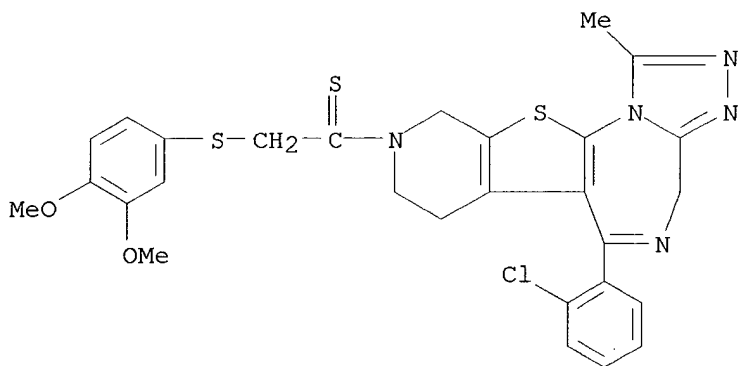
~~132579-32-9D~~, BN 50730, mixts. with anticholinergics

RL: BIOL (Biological study)

(drugs for treatment of bronchial asthma, synergistic)

RN 128672-07-1 CAPLUS

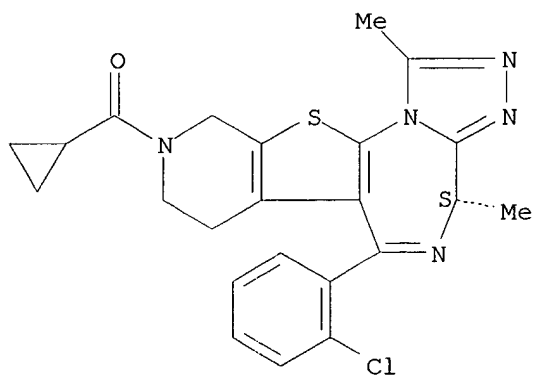
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 131614-02-3 CAPLUS

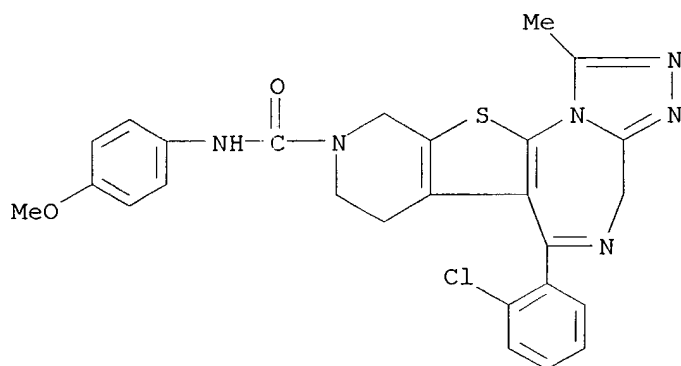
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



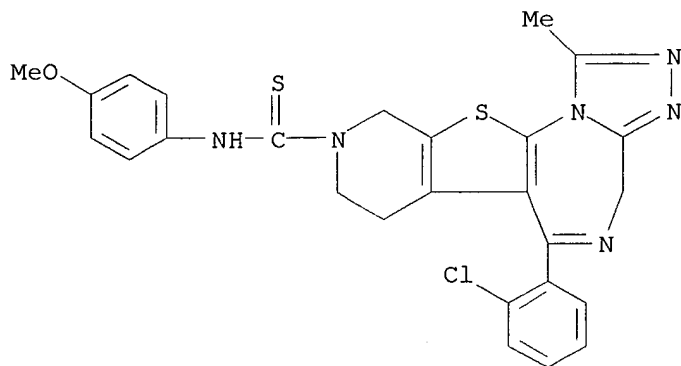
RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



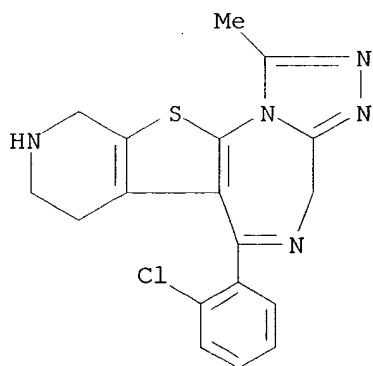
RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

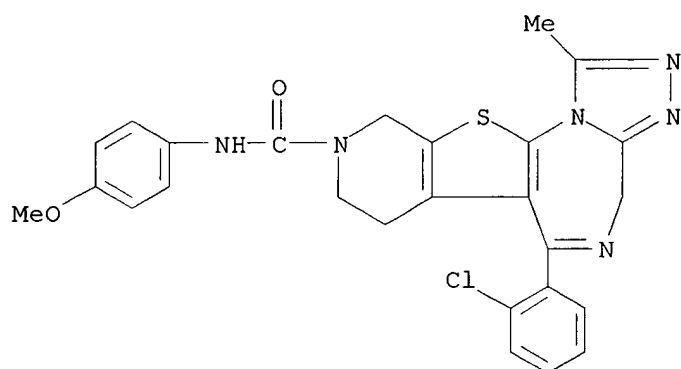


09/701,893

L23 ANSWER 53 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1994:152676 CAPLUS
 DN 120:152676
 TI Mass spectrometry and liquid chromatography/mass spectrometry of some derivatives of 6-(2-chlorophenyl)-1-methyl-7,8,9,10-tetrahydro-4H-pyrido[4',3'-4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepines
 AU Celma, C.
 CS Mass Spectrometry Dep., S. A. LASA Lab., Sant Feliu de Llobregat, E-08980, Spain
 SO Biol. Mass Spectrom. (1994), 23(1), 13-19
 CODEN: BIMSEH; ISSN: 1052-9306
 DT Journal
 LA English
 AB Electron impact and isobutane pos. and neg. chem. ionization mass spectra of some 6-(2-chlorophenyl)-1-methyl-7,8,9,10-tetrahydro-4H-pyrido[4',3'-4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine derivs. were detd. and their fragmentation pattern elucidated with the aid of D labeling and high-resoln. mass measurements. Liq. chromatog./mass spectrometry using both thermospray and particle beam interfaces of such compds. also were carried out. The most significant ions were derived from the thermal decompn. of the mols. giving the 6-(2-chlorophenyl)-1-methyl-7,8,9,10-tetrahydro-4H-pyrido[4',3'-4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine framework and an isothiocyanate or an isocyanate residue.
 IT **114800-58-7**, NHPTT **132418-35-0**, BN 50727
132579-32-9, BN 50730 **153339-88-9**, BN 50922
 RL: ANST (Analytical study)
 (mass spectrometry and liq. chromatog./mass spectrometry of)
 RN 114800-58-7 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

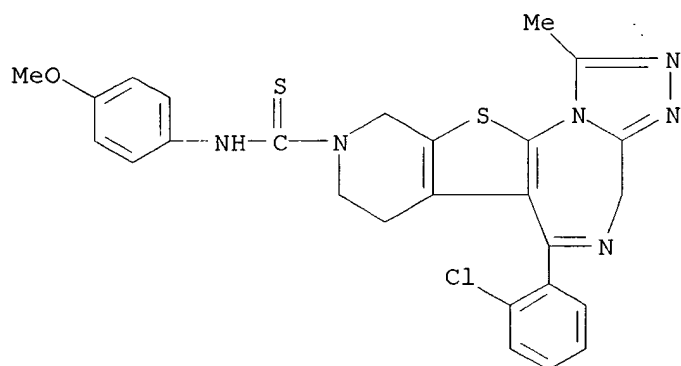


RN 132418-35-0 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



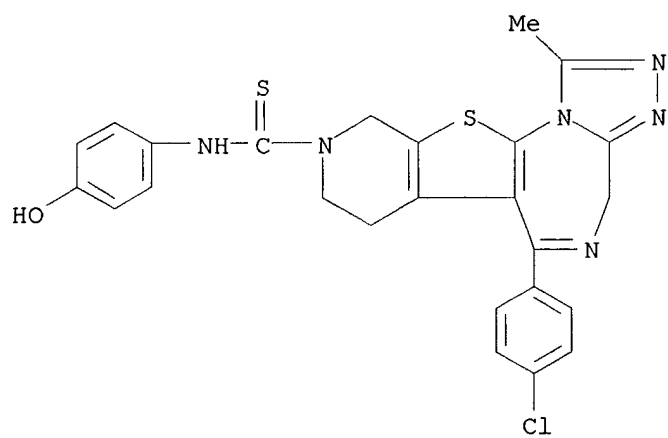
b₂

RN 132579-32-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



b₂

RN 153339-88-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 54 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1994:45861 CAPLUS

DN 120:45861

TI Total inhibition of PAF retinal effect by a pretreatment with a specific PAF antagonist (BN 50730) in rat

AU Doly, M.; Droy-Lefaix, M. T.; Bonhomme, B.; Braquet, P.

CS Lab. Biophys., Sch. Med., Clermont-Ferrand, 63001, Fr.

SO Int. Congr. Ser. - Excerpta Med. (1992), 998(Oxygen Radicals), 589-92

CODEN: EXMDA4; ISSN: 0531-5131

DT Journal

LA English

AB The PAF antagonist activity of BN 50730 was demonstrated on the model of isolated retina. The PAF effects on retinal function based on the concn. of BN 50730 administered per os inside the retina appear very remarkable. In these conditions, such a PAF antagonist may be used in therapy to prevent functional consequences of ocular inflammatory diseases.

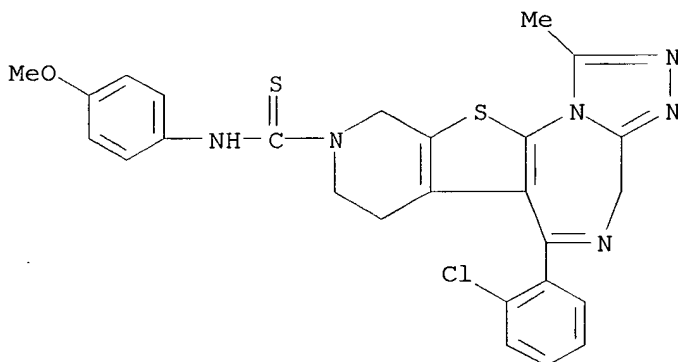
IT **132579-32-9**, BN 50730

RL: BIOL (Biological study)

(PAF retinal effect inhibition by)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



~~123~~ ANSWER 55 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1994:23005 CAPLUS

~~DN~~ 120:23005

TI Metabolic polymorphism of E6123 in rhesus monkey

AU Kusano, K.; Tanaka, S.; Ando, T.; Abe, Y.; Ida, S.; Yuzuriha, T.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SO Xenobiotica (1993), 23(6), 599-608

CODEN: XENOBH; ISSN: 0049-8254

DT Journal

LA English

AB The metabolic polymorphism of a new thienodiazepine platelet activating factor receptor antagonist (E6123) in rhesus monkey was studied in vivo and in vitro. After i.v. dosing of ¹⁴C-E6123, the levels of radioactivity in blood, plasma and red blood cells were higher in poor metabolizers (PMs) with AUC(0-24 h) values which were about 1.3-1.5 times higher than those in extensive metabolizers (EMs). After i.v. dosing of ¹⁴C-E6123, radioactivity was excreted rapidly by both EMs and PMs. However, EMs excreted the radioactivity mainly in urine whereas, for PMs, radioactivity was excreted fairly equally in urine and feces. In vivo and in vitro studies demonstrated that the metabolic polymorphism of E6123 in rhesus monkey is caused by a difference in the hydrolysis of an amide side chain. The results suggest that there are two types of the enzymes which metabolize E6123 by this route in EMs, but only one type in PMs. The low affinity enzyme in EMs might be the same as the enzyme in PMs, indicating that the metabolic polymorphism of E6123 in rhesus monkey could depend on the existence of a high affinity enzyme.

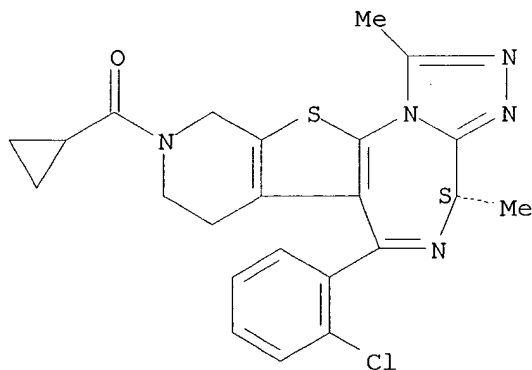
IT **131614-02-3**, E6123

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metab. of, in rhesus monkey, genetic polymorphism in)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



~~D23~~ ANSWER 56 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1994:23004 CAPLUS

~~DN~~ 120:23004

~~TI~~ Pharmacokinetics of a new thienodiazepine platelet activating factor receptor antagonist (E6123) in laboratory animals. Is there a metabolic polymorphism in the rhesus monkey?

~~AU~~ Kusano, K.; Tanaka, S.; Abe, Y.; Ida, S.; Yuzuriha, T.

~~CS~~ Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

~~SO~~ Xenobiotica (1993), 23(6), 589-98

CODEN: XENOBH; ISSN: 0049-8254

~~DT~~ Journal

~~LA~~ English

~~AB~~ The pharmacokinetics of E6123, a platelet activating factor receptor antagonist, were studied after i.v. and oral administration to rat, guinea-pig, dog and rhesus monkey. Plasma concns. of E6123 were detd. by HPLC with UV detection. After i.v. dosing (1 mg/kg), the plasma concn.-time curves fitted a two-compartment model. The half-lives for the terminal phases ($t_{1/2}$) in rat, dog, and guinea-pig showed very little inter-individual variation, but $t_{1/2}$ in the monkey varied more than four-fold. The distribution parameters were very similar in rat, dog and monkey (V_c and V_{ss} approx. 1.2 and 1.5 l/kg, resp.) but slightly higher values were found in the guinea-pig, which also showed the lowest plasma protein binding. After oral dosing (1 mg/kg), the max. plasma concns. were obtained within 0.3-3.0 h in all species. The half-life for each individual animal was almost the same as that after i.v. dosing. The mean bioavailabilities of E6123 in rat, guinea-pig and dog were about 65, 95 and 81%, resp., but the values for monkey were again highly variable (range 32-99%). The high variability in the monkey was confirmed by i.v. administration to a further 10 animals. The mean half-lives for the terminal phase in extensive metabolizers (EMs) and poor metabolizers (PMs) were approx. 1 and 4 h, resp. The rank order for total body clearance of E6123 was: rat > monkey (EMs) > dog > guinea-pig > monkey (PMs).

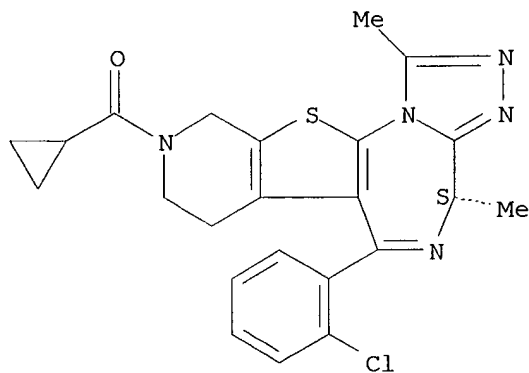
~~IT~~ 131614-02-3, E6123

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, species differences in)

~~RN~~ 131614-02-3 CAPLUS

~~CN~~ 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 57 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:610708 CAPLUS

DN 119:210708

TI Treatment of dysmenorrhea with PAF antagnoists

IN Kutter, Eberhard

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 8 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4200610	A1	19930715	DE 1992-4200610	19920113
	WO 9313776	A1	19930722	WO 1993-EP47	19930112

W: JP, US

PW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI DE 1992-4200610 19920113

OS MARPAT 119:210708

AB PAF antagonists are drugs for the treatment of dysmenorrhea, esp. primary dysmenorrhea (no data). Suitable PAF antagonists are alprazolam, dilthiazem, brotizolam, hetrazepine derivs., etc. Formulation examples are given. The PAF antagonist 2-[4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-2-yl]ethane-1-carboxylic acid morpholide was prepd. by the reaction of 2-[4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f][1,4]diazepin-2-yl]ethane-1-carboxylic acid with N-hydroxybenzotriazole and morpholine, in abs. DMF.

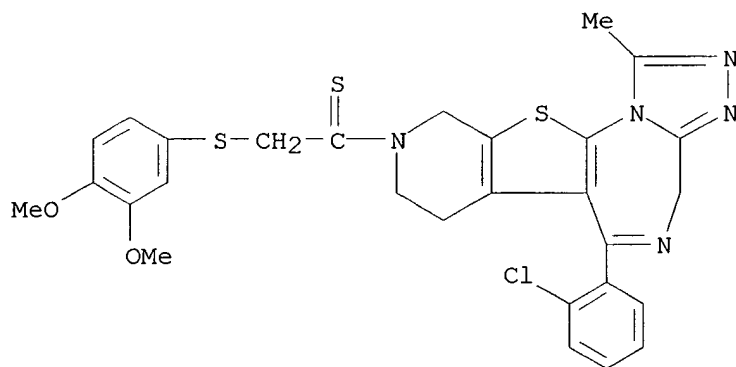
IT **128672-07-1**, BN-50739 **131614-02-3**, E-6123**132579-32-9**, BN-50730 **133686-55-2**, BN-50727

RL: BIOL (Biological study)

(PAF antagonist, dysmenorrhea treatment by)

RN 128672-07-1 CAPLUS

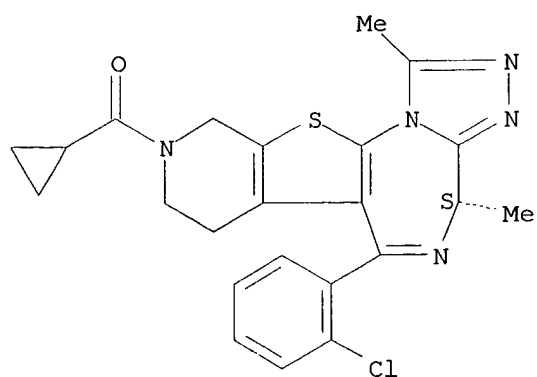
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

RN ~~131614-02-3~~ CAPLUS

CN ~~4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)~~

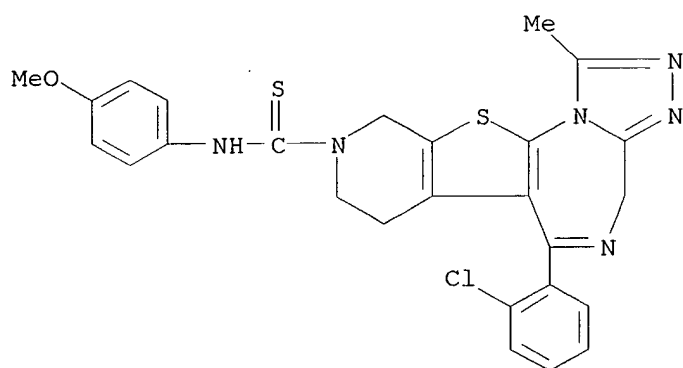
Absolute stereochemistry.

09/701,893



RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



RN 133686-55-2 CAPLUS

L23 ANSWER 58 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:508329 CAPLUS

DN 119:108329

TI Pharmacokinetic studies of (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,4-a][1,4]diazepine (E6123). (I). Absorption, distribution, metabolism, excretion and identification of metabolites in beagle dogs

AU Kusano, Kazutomi; Tanaka, Shigeru; Kosaki, Teruya; Miyazawa, Shuhei; Tadano, Kyoichi; Yuzurha, Teruaki

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

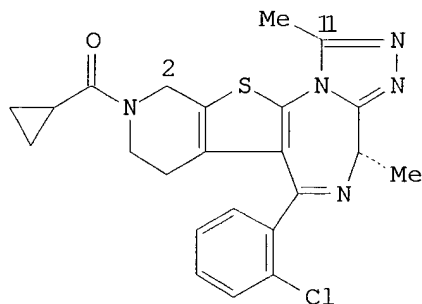
SO Yakubutsu Dotai (1993), 8(2), 221-37

CODEN: YADOEL; ISSN: 0916-1139

DT Journal

LA Japanese

GI



AB The absorption, distribution, metab., excretion and metab. of the PAF receptor antagonist E6123 (I) were studied in beagle dogs after a single oral administration. After oral administration, the radioactivity in blood, plasma and hematocytes reached their C_{max}s at 2.3, 3.0 and 2.0 h, resp. And then the radioactivity decreased two-exponentially with their t_{1/2λ} and t_{1/2} of 6.3 h and 33.9 h in blood, 4.9 h and 38.7 h in plasma, 3.0 h and 18.7 h in hematocytes, resp. The AUCs in blood, plasma and hematocytes were 3952, 3745, 4167 ng equiv..cntdot.h/mL, resp. After oral administration, C_{max} of unchanged drug in plasma was reached at 1.3 h and then decreased rapidly with t_{1/2} of 1.7 h. The AUC was 330 ng.cntdot.h/mL. In vitro plasma protein binding of ¹⁴C-E6123 varied from 57 to 59% at the range of concn. from 10 to 1000 ng/mL. After oral administration, the in vivo plasma protein binding of radioactivity was approx. 59 and 85% for plasma samples collected at 0.75 and 8 h, resp. After oral administration, the radioactivity in almost all tissues were the same or higher than that of plasma indicating that ¹⁴C-E6123 had an increased high affinity for tissues. The radioactivity in the tissues, except eye, disappeared fast. The level of radioactivity in the lung as the target organ was 1.8 times higher than that in plasma at 2 h after administration. Furthermore, the compn. of metabolites of E6123 in plasma and lung was almost the same and the unchanged drug was the main compd. Approx. 42 and 47% of radioactivity was excreted in urine and feces during 48 h after oral administration, resp. At least seven metabolites were found in urine and feces with a small quantity of unchanged drug. Main metabolic pathways were shown to be as follows; (1) oxidn. of Me group at the 11-position, (2) oxidn. of carbon 2 and (3) hydrolysis of side chain.

09/701,893

IT 130311-76-1 150363-85-2

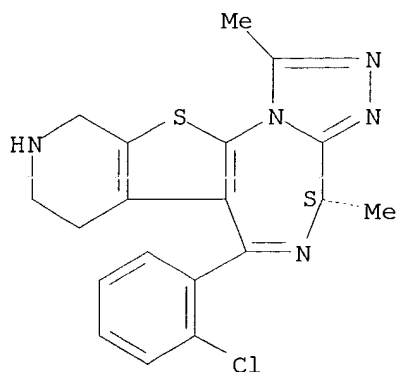
RL: FORM (Formation, nonpreparative)

(formation of, as PAF receptor antagonist E 6123 metabolite)

RN 130311-76-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (S)- (9CI) (CA
INDEX NAME)

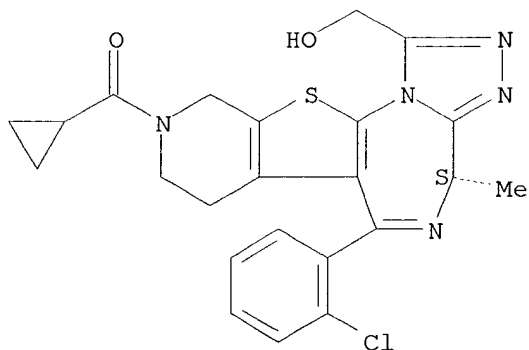
Absolute stereochemistry.



RN 150363-85-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-1-
methanol, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-4-
methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 131614-02-3, E 6123

RL: BIOL (Biological study)

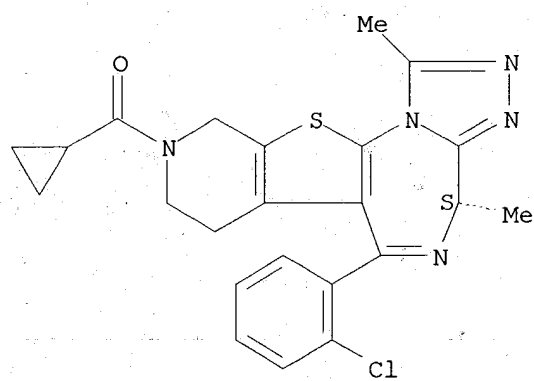
(pharmacokinetics and metab. of)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



09/701,893

L23 ANSWER 59 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:240950 CAPLUS

DN 118:240950

TI Use of hetrazepinoid platelet-activating factor antagonists for treatment of allergic rhinitis

IN Blank, Burkhard; Brecht, Hans Michael

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 8 pp.

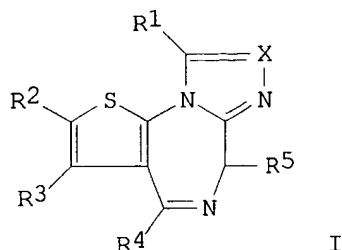
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4128581	A1	19930304	DE 1991-4128581	19910828
OS	MARPAT 118:240950				
GI					



AB Hetrazepinoids I [R1 = H, C1-4 alkyl or haloalkyl, halo, C3-6 cycloalkyl; R2 = (substituted) amino, Ph, C(:O)R6, aminoalkyl, phenylalkyl, etc.; R3 = H, or R2R3 complete a 5- or 6-membered ring; R4 = (substituted) Ph; R5 = H, OH, (substituted) C1-4 alkyl; R6 = amino, OH, C1-4 alkoxy; X = N, CH] are useful for treatment of allergic rhinitis (no data). Thus, hard gelatin capsules were prepd. contg. I (e.g. Web 2086) 50.0, corn starch 268.5, and Mg stearate 1.5 mg/each.

IT **128672-07-1**, BN 50739 **131614-02-3**, E 6123

132579-32-9, BN 50730

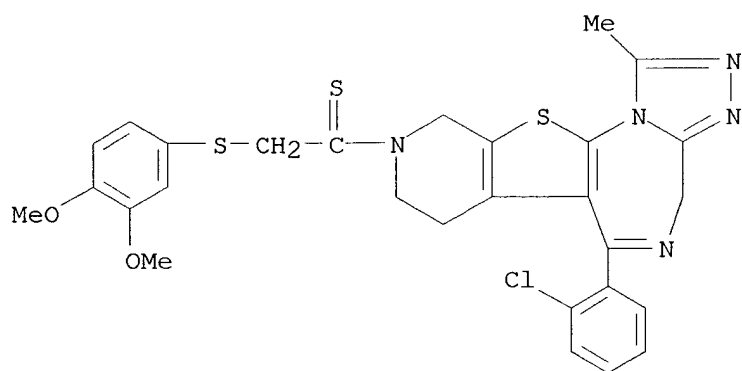
RL: BIOL (Biological study)

(hay fever treatment with)

RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

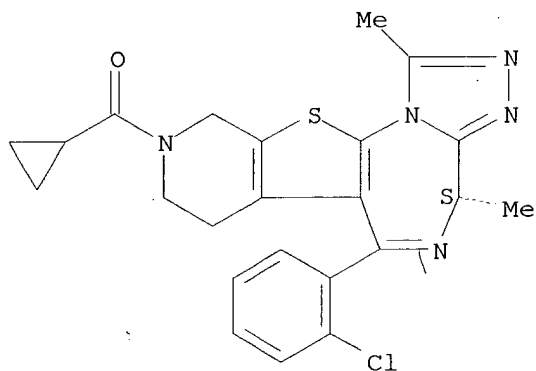
09/701,893



RN 131614-02-3 CAPLUS

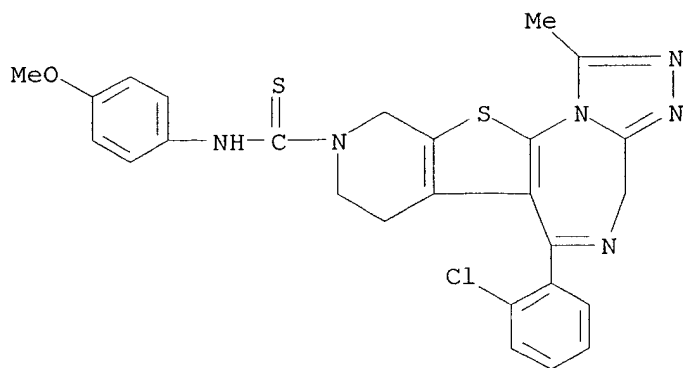
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
1-methyl-, (9CI) (CA INDEX NAME)



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09/701,893

~~123~~ ANSWER 60 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:109761 CAPLUS

DN 118:109761

TI Granules coated with pharmaceuticals and polymers

IN Nitta, Katsumi; Aoki, Shigeru; Uesugi, Keizo; Ozawa, Hiroshi

PA Eisai Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

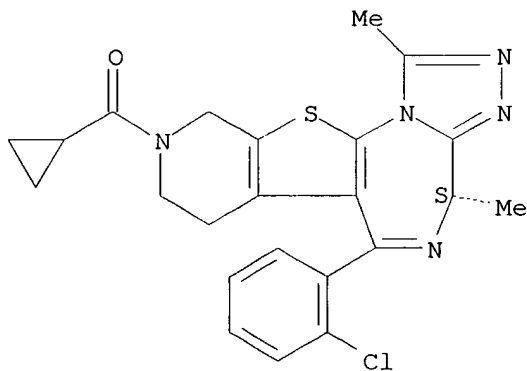
DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04312523	A2	19921104	JP 1991-103600	19910410
AB	Granules prep'd. by coating core materials with pharmaceuticals, followed by polymers and tablets contg. the granules are claimed. The granules prevent bitterness and astringency, and reduce gritty feeling in the mouth. Thus, 1800 g potato starch and 100 mL EtOH contg. 20 g S-(+)-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido-[4,3:4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine were mixed, dried at 60.degree. for 8 h, sifted, mixed with Mg stearate, and spray-coated with 2% aminoalkyl methacrylate copolymer EtOH soln. to give coated granules, which (300 g) were mixed with lactose 480, sugar 240, mannitol 240, and corn starch 150 g, granulated and sprayed with a 2% hydroxypropyl cellulose aq. soln., and sifted to give granules.				
IT	131614-02-3 RL: BIOL (Biological study) (nonpareils coating with, for manuf. of granules)				
RN	131614-02-3 CAPLUS				
CN	4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



09/701,893

~~13~~ ANSWER 61 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:66911 CAPLUS

DN 118:66911

TI Pharmaceutical granules and tablets containing drug particles coated with polymers

IN Nitsuta, Katsumi; Aoki, Shigeru; Uesugi, Keizo; Ozawa, Hiroshi

PA Eisai Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

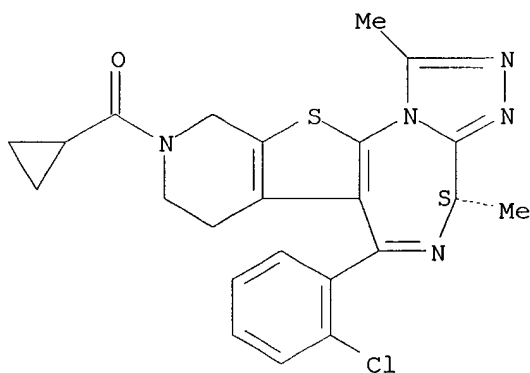
DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04282312	A2	19921007	JP 1991-67693	19910308
AB	Particles which comprise core materials successively coated with drugs and polymers, and granules and tablets manufd. from the particles are claimed. The particles are free from bitter and astringent taste and give no rough texture in the mouth. Potato starch (1800 g) was treated with a 100 mL EtOH soln. contg. 20 g (S)-(+)-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4,3:4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, and the compn. was dried at 60.degree. for 8 h. The obtained powder was mixed with Mg stearate and spray-coated with an EtOH soln. of aminoalkyl methacrylate copolymer to give coated particles. A mixt. contg. the coated particles 300, lactose 480, sucrose 240, mannitol 240, and corn starch 150 g was granulated while spraying an aq. hydroxypropyl cellulose soln. to give granules.				
IT	131614-02-3				
	RL: BIOL (Biological study)				
	(pharmaceutical particles of, polymer coating for)				
RN	131614-02-3 CAPLUS				
CN	4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



L23 ANSWER 62 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1993:22262 CAPLUS

DN 118:22262

TI Preparation of thieno[3,2-f][1,2,4] triazolo[4,3-a][1,4]diazepines and related compounds as platelet activating factor antagonists

IN Weber, Karl Heinz; Stransky, Werner; Kuefner-Muehl, Ulrike; Heuer, Hubert; Birke, Franz

PA Boehringer Ingelheim KG, Germany

SO Ger. Offen., 29 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4107521	A1	19920910	DE 1991-4107521	19910308
	EP 503471	A1	19920916	EP 1992-103739	19920305
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	CA 2062456	AA	19920909	CA 1992-2062456	19920306
	JP 05065288	A2	19930319	JP 1992-48930	19920306
	US 5753647	A	19980519	US 1994-350196	19941205
PRAI	DE 1991-4107521		19910308		
	US 1992-848575		19920309		
	US 1993-152045		19931112		

OS MARPAT 118:22262

GI For diagram(s), see printed CA Issue.

AB Title compds. [I; R1 = H, halo, (HO- or halo-substituted) alkyl, cyclopropyl, cyclobutyl; R2, R3 = H, Me, CF3, HOCH2; R4 = (substituted) Ph, pyridyl, thienyl; X = N, CH; A = Q1, Q2, Q3; B = CH2, CH2CH2; R5 = (substituted) alkyl, (substituted) aryl, or arylmethyl, arylethyl; R6 = H, (substituted) alkyl, PhCH2; Z = alkylene; Z1 = alkylene, bond; m, n = 1-3; m + n = 2-4], were prepd. Thus, 4-piperidine.HCl was acylated with 4-ClC6H4COCl in refluxing THF contg. K2CO3; the product was cyclocondensed with o-chlorocycanoacetophenone and S in DMF/Et3N to give 2-amino-3-(2-chlorobenzoyl)-6-(4-chlorobenzoyl)tetrahydropyrido[2,3-c]thiophene. This was acylated with MeCHBrCOCl followed by amination with NH3 and cyclization in refluxing PhMe contg. SiO2 with removal of H2O to give 3-(4-chlorobenzoyl)-6-(2-chlorophenyl)-8-methyl-2,3,4,5-tetrahydro-4H-pyrido[4,2:4',5']thieno[3,2-f][1,4]diazepin-9-one. This was sulfated with P2S5 in glyme contg. NaHCO3 and the resulting thione was stirred with N2H4 in THF followed by reflux with (EtO)3CMe in EtOH to give title compd. II. (-)-II inhibited 3H-platelet activating factor binding to human blood platelets with Ki = 1.9 nM. Dosage forms were prepd. contg. the 3-(3-chlorobenzoyl) analog of II.

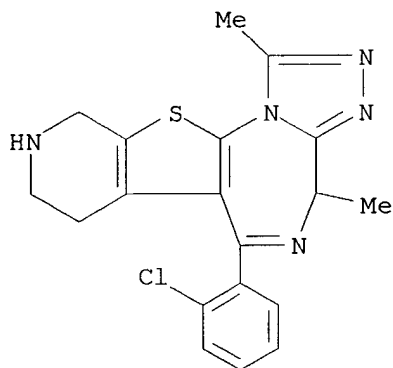
IT **130311-75-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as intermediate for platelet activating factor antagonist)

RN 130311-75-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX NAME)



Proviso
a

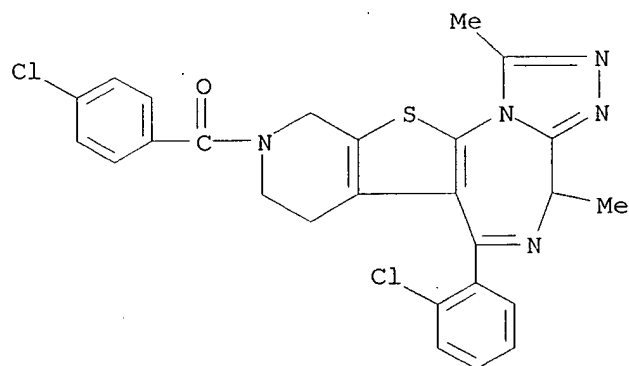
IT 144947-24-0P 144947-25-1P 144947-26-2P
144947-27-3P 144947-28-4P 144947-29-5P
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144947-41-1P 144947-42-2P 144947-43-3P
144947-44-4P 144947-46-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as platelet activating factor antagonist)

RN 144947-24-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 9-(4-chlorobenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (9CI) (CA INDEX NAME)



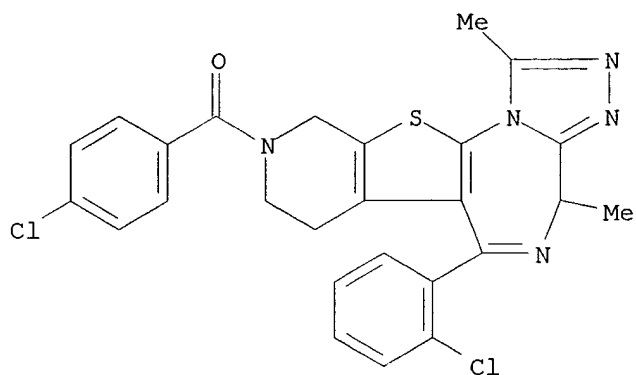
Proviso
b (11/11/11)

RN 144947-25-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 9-(4-chlorobenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

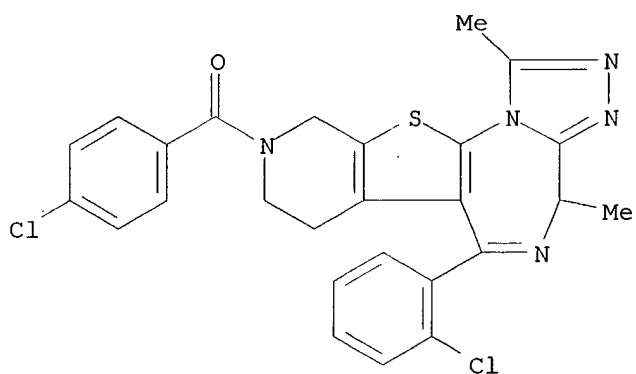
09/701,893



RN 144947-26-2 CAPLUS

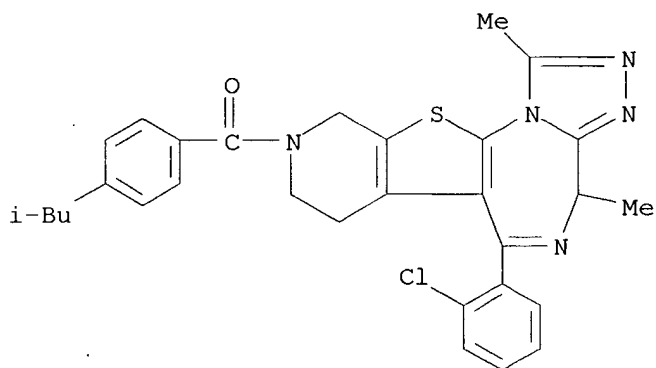
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-(4-chlorobenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-,
(-)-(9CI) (CA INDEX NAME)

Rotation (-).



RN 144947-27-3 CAPLUS

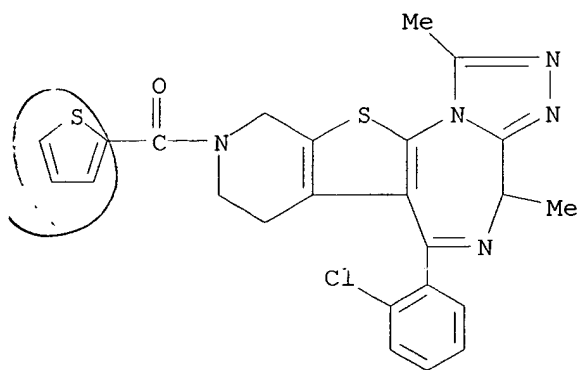
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[4-(2-
methylpropyl)benzoyl]-(-)(9CI) (CA INDEX NAME)



09/701,893

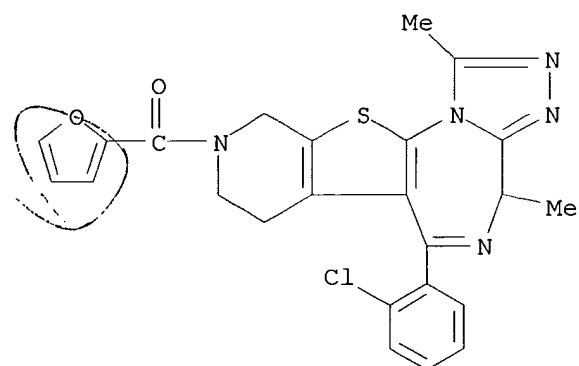
RN 144947-28-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-(2-thienylcarbonyl)-
(9CI) (CA INDEX NAME)



RN 144947-29-5 CAPLUS

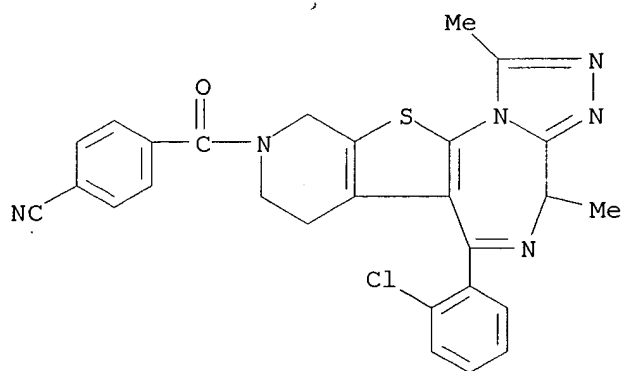
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(2-furanylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-
(9CI) (CA INDEX NAME)



RN 144947-30-8 CAPLUS

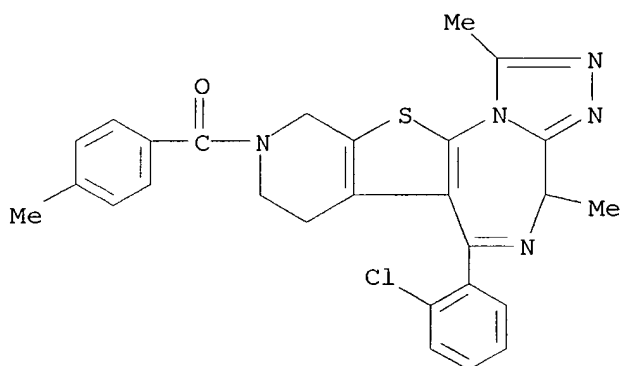
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(4-cyanobenzoyl)-7,8,9,10-tetrahydro-1,4-dimethyl-
(9CI) (CA INDEX NAME)

09/701,893



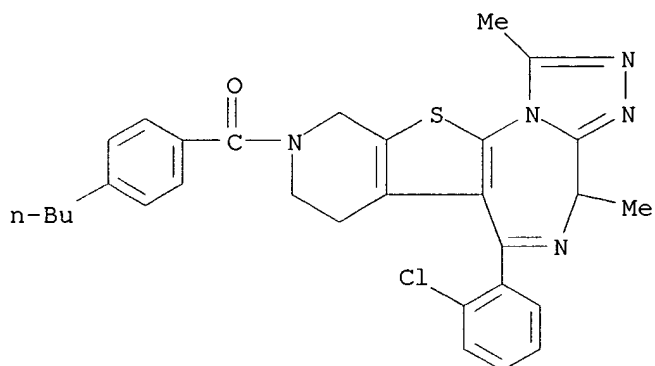
RN 144947-31-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-(4-methylbenzoyl)-
(9CI) (CA INDEX NAME)



RN 144947-32-0 CAPLUS

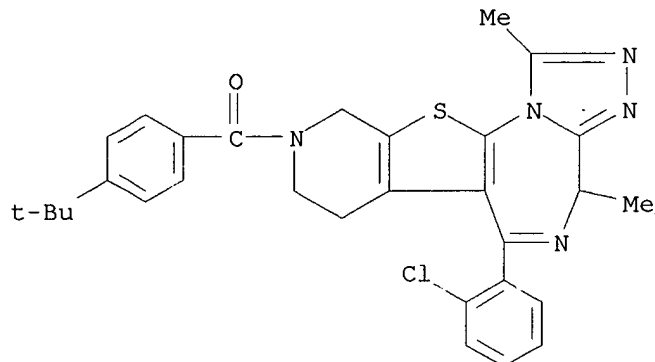
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-(4-butylbenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-
(9CI) (CA INDEX NAME)



09/701,893

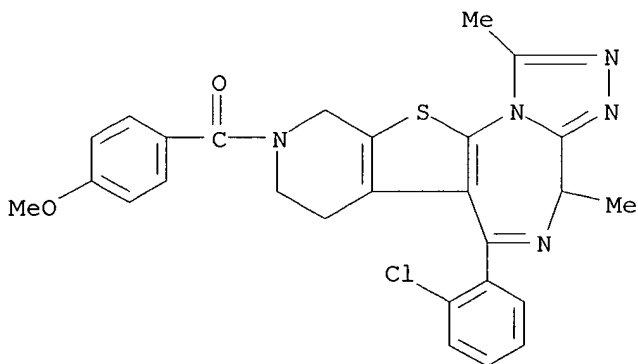
RN 144947-33-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[4-(1,1-dimethylethyl)benzoyl]-7,8,9,10-tetrahydro-
1,4-dimethyl- (9CI) (CA INDEX NAME)



RN 144947-34-2 CAPLUS

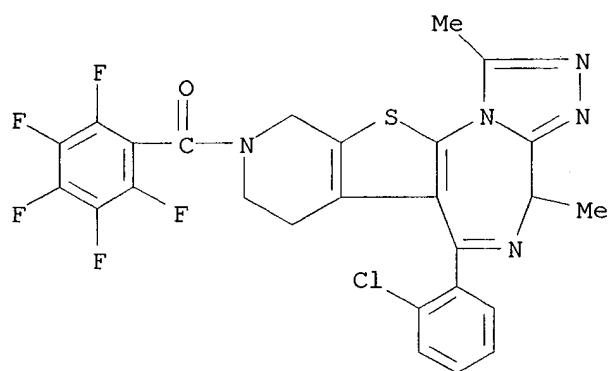
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-(4-methoxybenzoyl)-1,4-dimethyl-
(9CI) (CA INDEX NAME)



RN 144947-35-3 CAPLUS

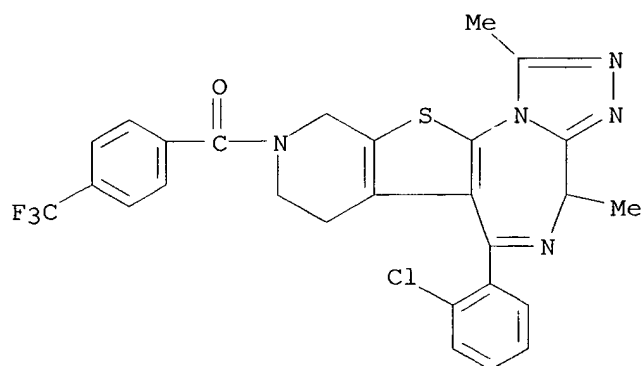
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-(pentafluorobenzoyl)-
(9CI) (CA INDEX NAME)

09/701,893



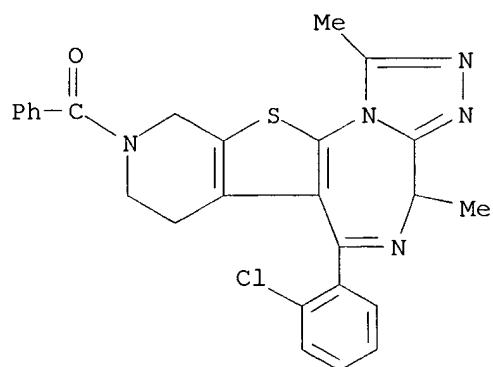
RN 144947-36-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-[4-
(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)



RN 144947-37-5 CAPLUS

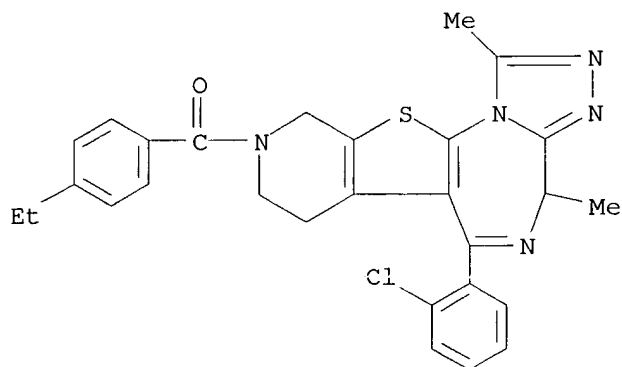
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-benzoyl-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA
INDEX NAME)



09/701,893

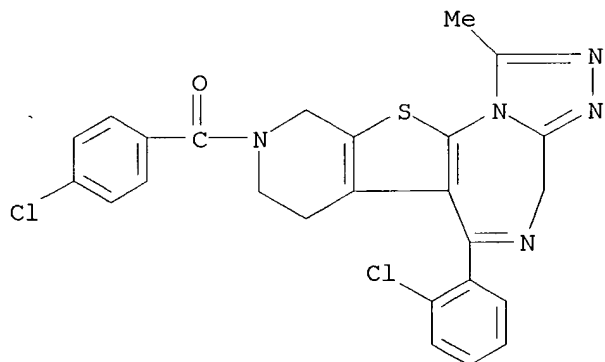
RN 144947-40-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(4-ethylbenzoyl)-7,8,9,10-tetrahydro-1,4-dimethyl-
(9CI) (CA INDEX NAME)



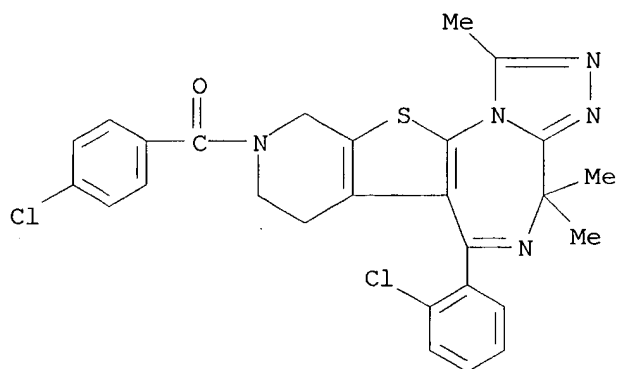
RN 144947-41-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-(4-chlorobenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI)
(CA INDEX NAME)

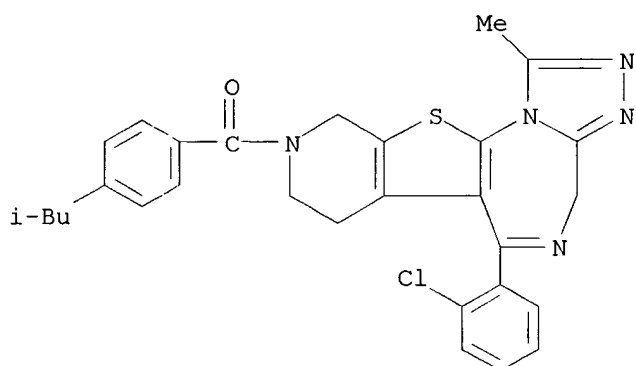


RN 144947-42-2 CAPLUS

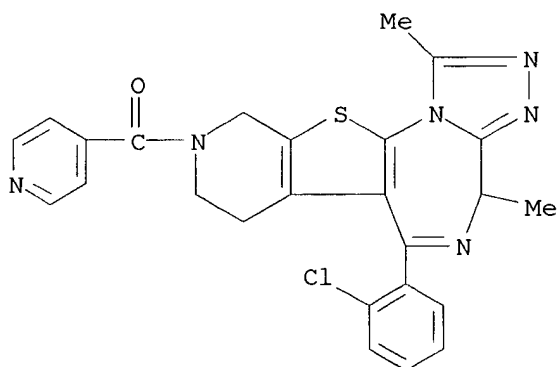
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
9-(4-chlorobenzoyl)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4,4-trimethyl-
(9CI) (CA INDEX NAME)



RN 144947-43-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[4-(2-
 methylpropyl)benzoyl]- (9CI) (CA INDEX NAME)



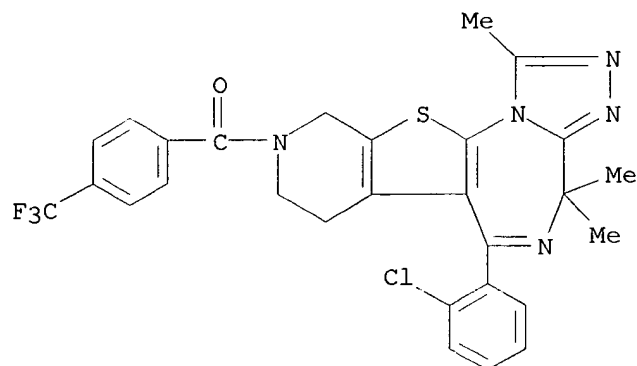
RN 144947-44-4 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-9-(4-
 pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



09/701,893

RN 144947-46-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4,4-trimethyl-9-[4-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)



L23 ANSWER 63 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:590035 CAPLUS

DN 117:190035

TI Histamine secretion from mast cells stimulated with platelet activating factor (PAF)

AU Mustafa, S. B.; Pearce, F. L.

CS Dep. Chem., Univ. Coll. London, London, WC1H 0AJ, UK

SO Agents Actions (1992), (Spec. Conf. Issue), C265-C267

CODEN: AGACBH; ISSN: 0065-4299

DT Journal

LA English

AB Platelet activating factor (PAF) produced a dose-dependent release of histamine from rat peritoneal mast cells. The release was noncytotoxic at 5 mM but cytotoxic at a concn. >10 .mu.M. Isolated tissue mast cells of the rat, guinea pig, and man showed varying responses to PAF but the release was again generally cytotoxic. The noncytotoxic release from rat serosal mast cells stimulated with low concns. of PAF was potently inhibited by phosphodiesterase inhibitors, cAMP-active drugs, and the naturally occurring flavonoid quercetin. The release was also selectively inhibited by the specific PAF antagonist BN 50730, but not by BN 52021 or WEB 2086. These findings suggest that PAF may interact with the mast cell membrane to produce mediator release, rather than acting via a specific receptor.

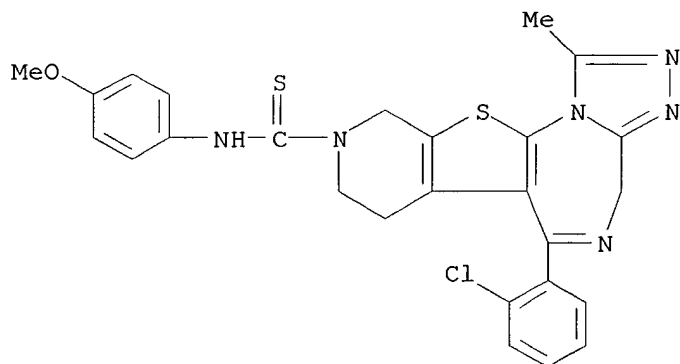
IT 132579-32-9, BN 50730

RL: BIOL (Biological study)

(platelet-activating factor stimulation of histamine release from mast cell inhibition by)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 64 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1992:448619 CAPLUS
 DN 117:48619
 TI Preparation of new thienotriazolodiazepine derivatives as drugs
 PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.
 SO Neth. Appl., 26 pp.
 CODEN: NAXXAN
 DT Patent
 LA Dutch
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	NL 9000627	A	19911016	NL 1990-627	19900319
OS	MARPAT 117:48619				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds., tetrahydropyrido-fused thienotriazolodiazepine derivs. [I; Y = O or S; R = (a) straight-chain lower, i.e., C.ltoreq.5-, alkenyl, straight-chain or branched C.ltoreq.20-alkyl, or C.ltoreq.6-cyclic alkyl, (b) aryl- or heteroaryl-substituted, straight-chain C.ltoreq.5-alkyl, which aryl may be substituted with Me, (c) Ph substituted with .gtoreq.1 C.ltoreq.5-alkyl or -alkoxy groups, phenoxy, C.ltoreq.5-alkylsulfonyl, F or Cl, or CF₃, (d) heteroatom-contg. condensed bicyclic group, or (e) a sulfonyl group substituted with Ph or heteroaryl or condensed bicyclic group], are prepd. by acylation of the pyrido N of thienodiazepine compds. II (Y as above), under N and reflux, with a stoichiometrically small excess of a suitable iso(thio)cyanate deriv. R-N:C:Y in a protic solvent for 0.5-24 h, after which the resulting compd. III (both Y as above) is reacted at 0.degree. to ambient temp., under N and reflux, with a stoichiometrically small excess of H₂NNH₂.cntdot.H₂O for 5 min to .apprx.1 h, after which the resulting compd., having general formula III [Y (on ring) = NHNH₂], is reacted at room temp. in a protic solvent, under N, with 4 stoichiometric equivs tri-Et orthoacetate for 15 min to 3 h, after which the mixt. is refluxed for 0.5-5 h. These compds. are nontoxic when orally administered to mice in amts. of 1 g/kg, although a few (listed) are toxic when administered i.p., and they are of interest as antiasthmatics, antiallergics, and digestive tract-protecting agents. The prepn. of 6-(2-chlorophenyl)-9-[4-(methoxy)phenylthiocarbamoyl]-7,8,9,10-tetrahydro-1-methyl-4H-pyrido[4',3':4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]diazepine is given, and 35 addnl. I are listed. The 36 I were tested for inhibition of PAF-induced platelet aggregation and inhibition of antagonist binding to benzodiazepine receptors, and 12 were active against PAF-induced bronchoconstriction in test animals.

IT 132418-35-0P 132418-36-1P 132418-37-2P
 132418-38-3P 132418-39-4P 132418-40-7P
 132418-41-8P 132418-42-9P 132418-43-0P
 132418-44-1P 132418-45-2P 132418-46-3P
 132418-47-4P 132418-48-5P 132418-49-6P
 132418-50-9P 132418-51-0P 132418-52-1P
 132418-53-2P 132418-54-3P 132418-55-4P
 132418-56-5P 132418-58-7P 132418-59-8P
 132418-60-1P 132418-61-2P 132418-62-3P
 132418-64-5P 132442-67-2P 138192-67-3P

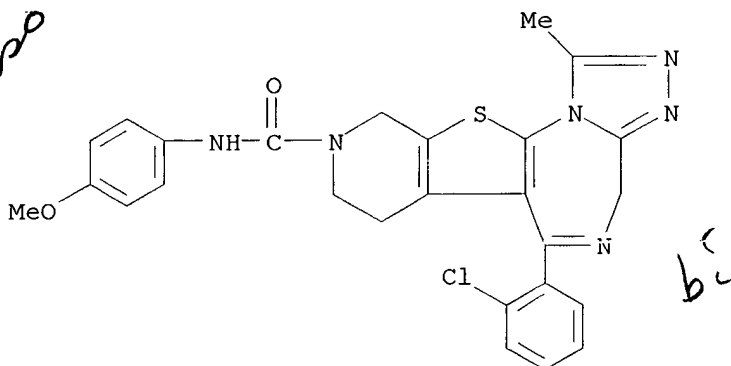
09/701,893

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiasthmatic and antiallergic)

RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-
methyl- (9CI) (CA INDEX NAME)

proviso

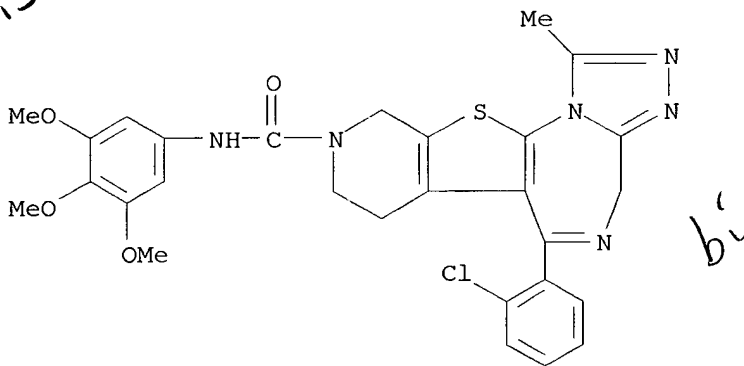


RN 132418-36-1 CAPLUS

RN 132418-37-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-
trimethoxyphenyl)- (9CI) (CA INDEX NAME)

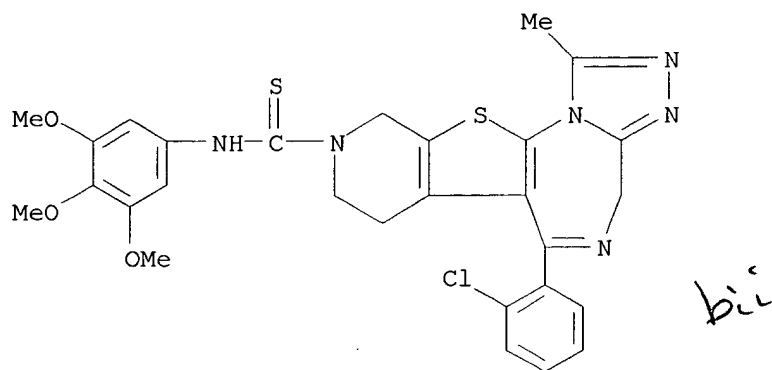
proviso



RN 132418-38-3 CAPLUS

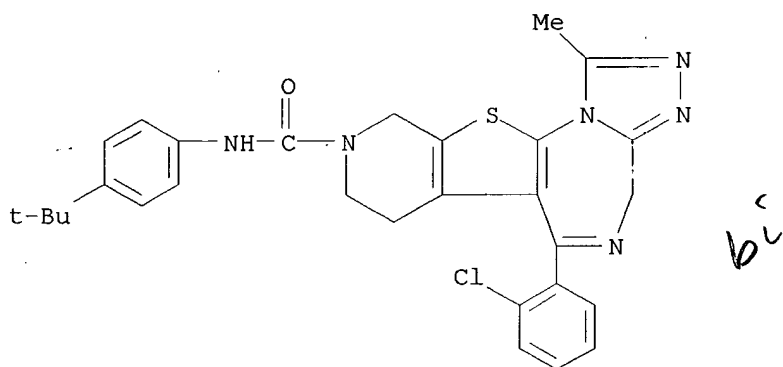
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-
trimethoxyphenyl)- (9CI) (CA INDEX NAME)

09/701,893



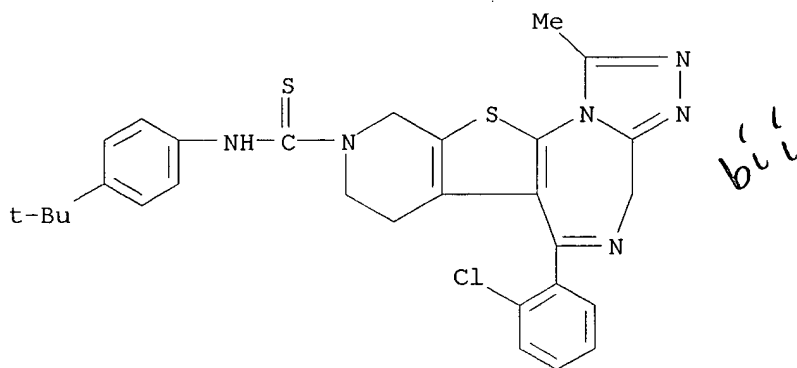
RN 132418-39-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-40-7 CAPLUS

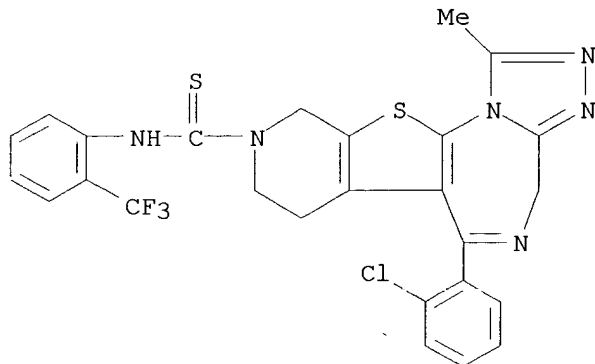
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-[4-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

RN 132418-41-8 CAPLUS

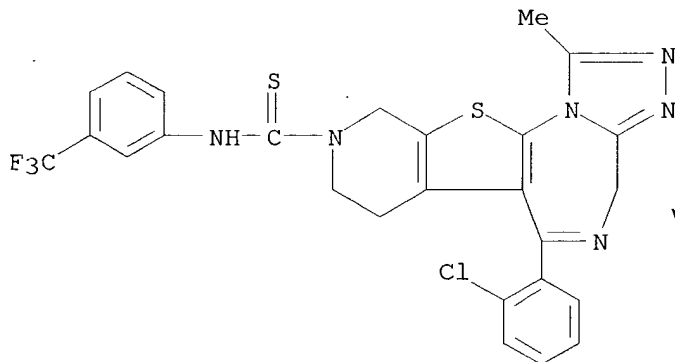
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



bii

FN 132418-42-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

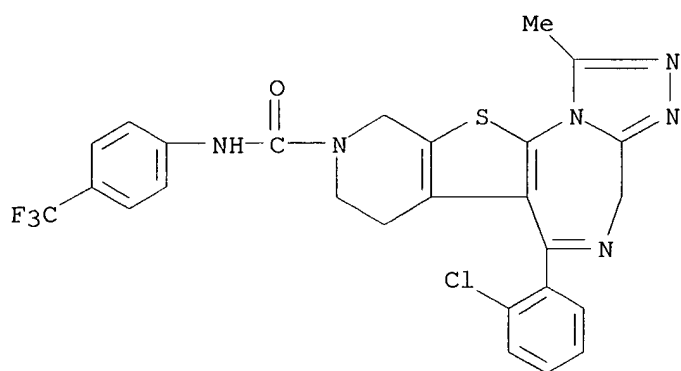


bii

RN 132418-43-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

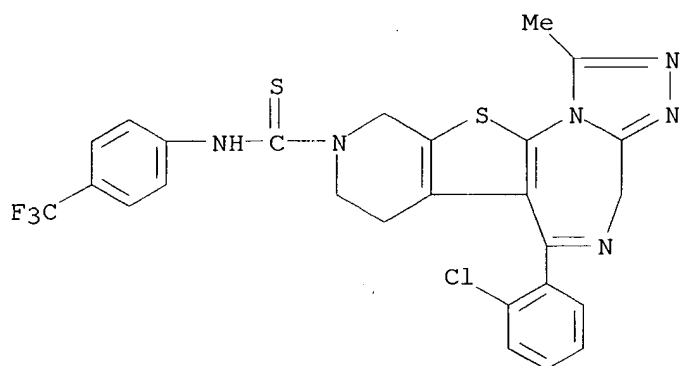
09/701,893



b₁

RN 132418-44-1 CAPLUS

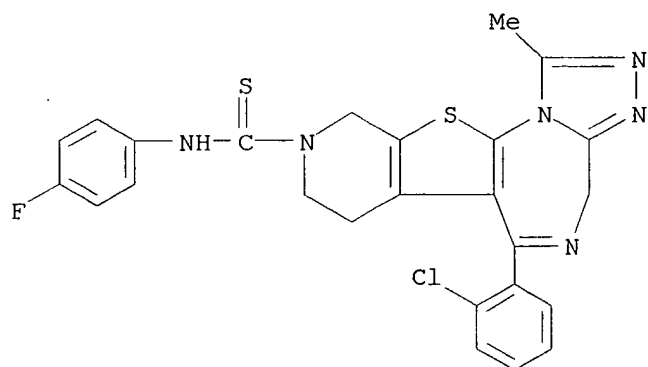
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



b₁

RN 132418-45-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-fluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

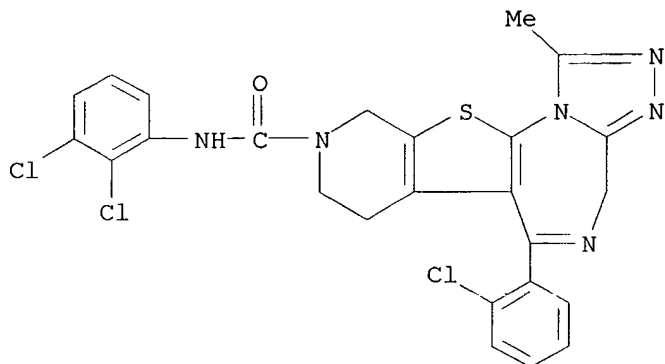


b₁

09/701,893

RN 132418-46-3 CAPLUS

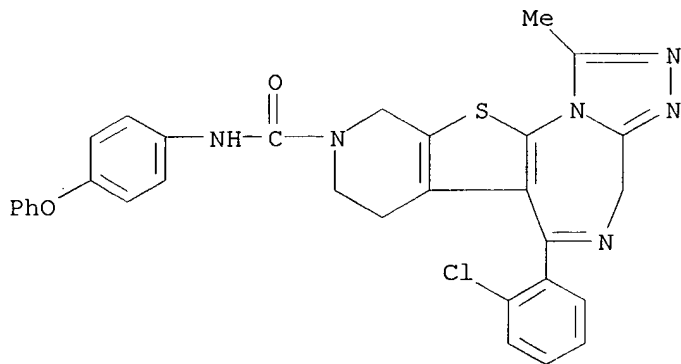
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,3-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



bi

RN 132418-47-4 CAPLUS

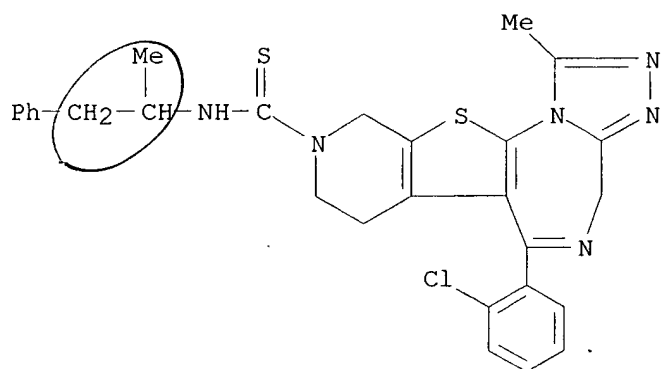
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



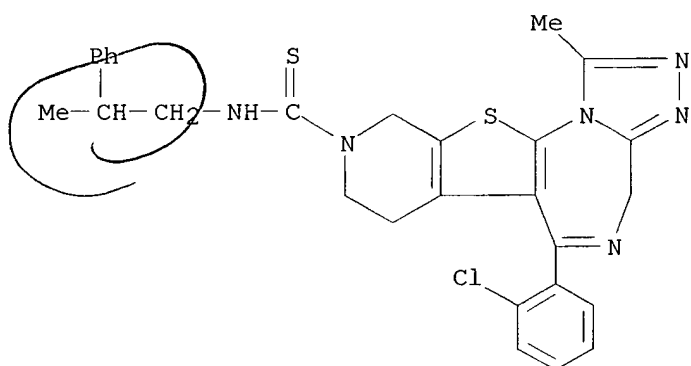
bi)

RN 132418-48-5 CAPLUS

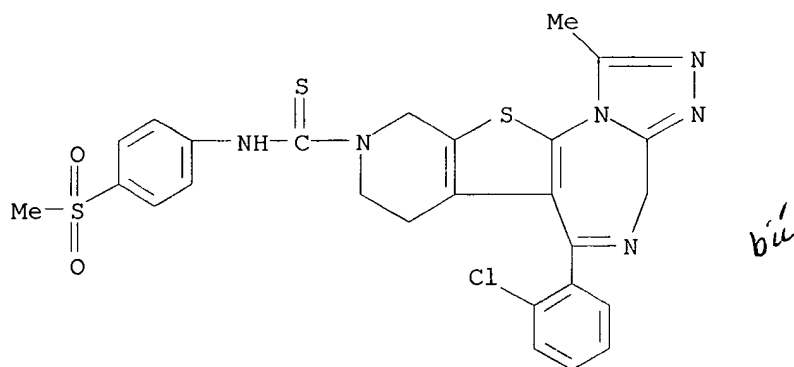
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1-methyl-2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 132418-49-6 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-phenylpropyl)- (9CI) (CA INDEX NAME)



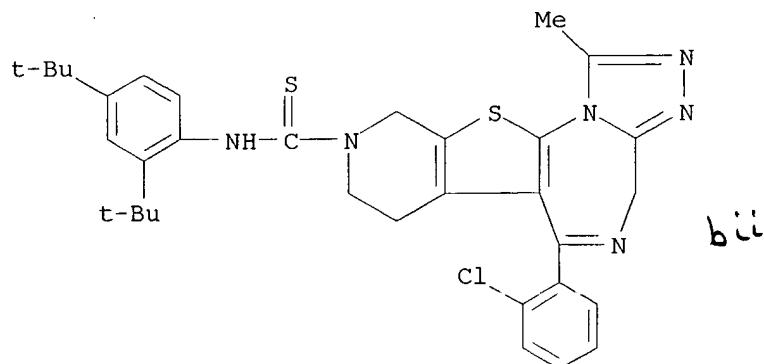
RN 132418-50-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



09/701,893

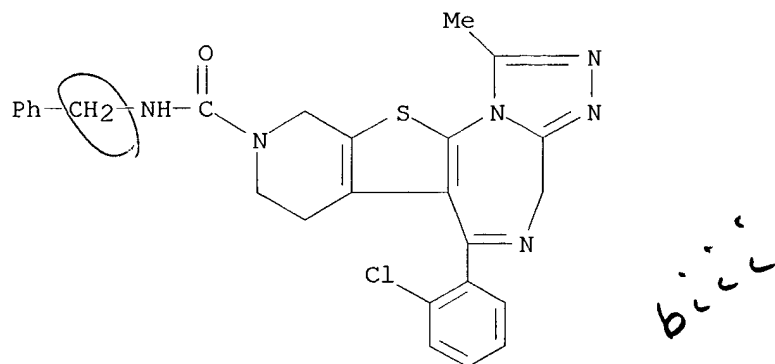
RN 132418-51-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[2,4-bis(1,1-dimethylethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-52-1 CAPLUS

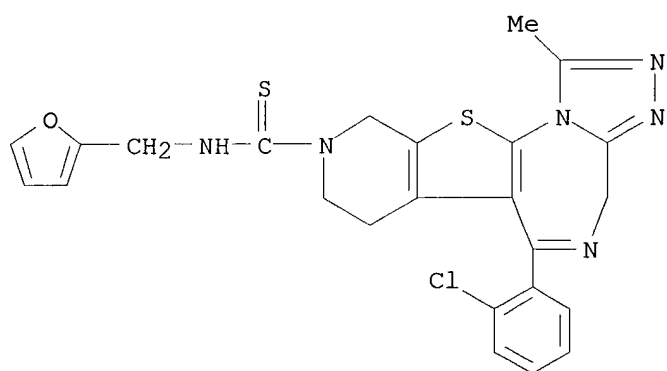
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 132418-53-2 CAPLUS

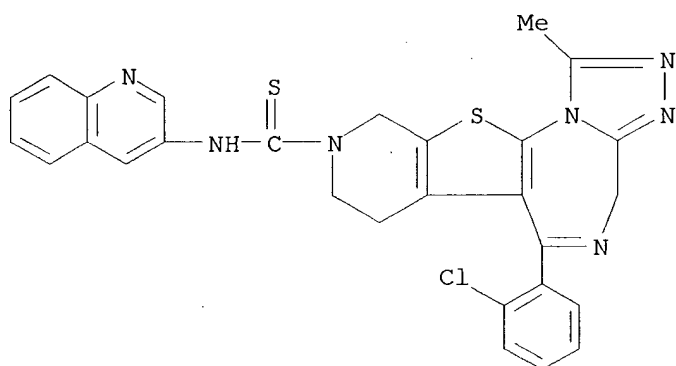
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylmethyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



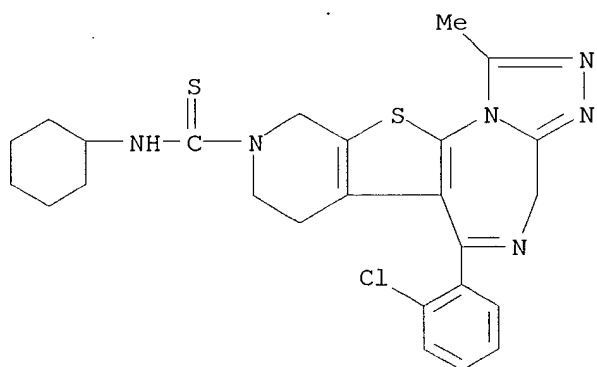
RN 132418-54-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-3-quinoliny- (9CI) (CA INDEX NAME)



RN 132418-55-4 CAPLUS

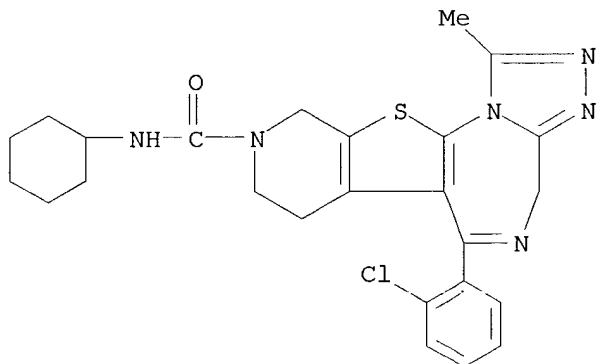
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

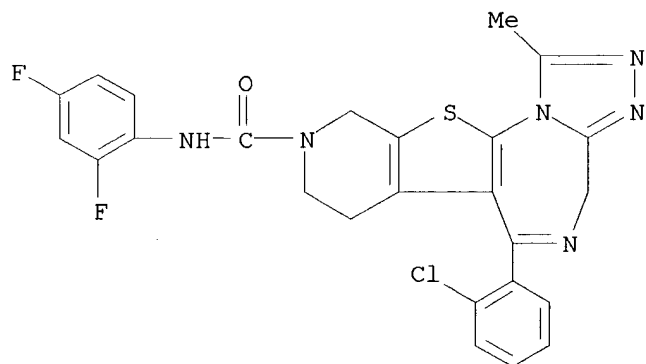
RN 132418-56-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl-(9CI) (CA INDEX NAME)



RN 132418-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,4-difluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

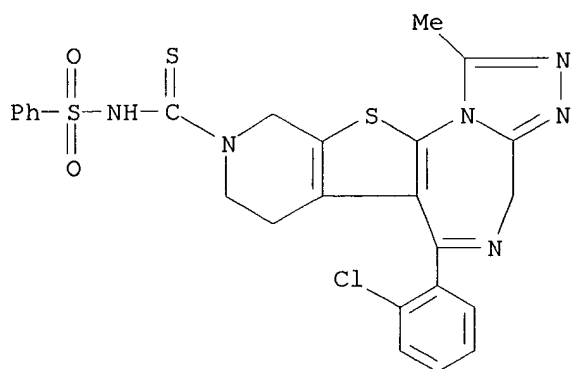


b.i)

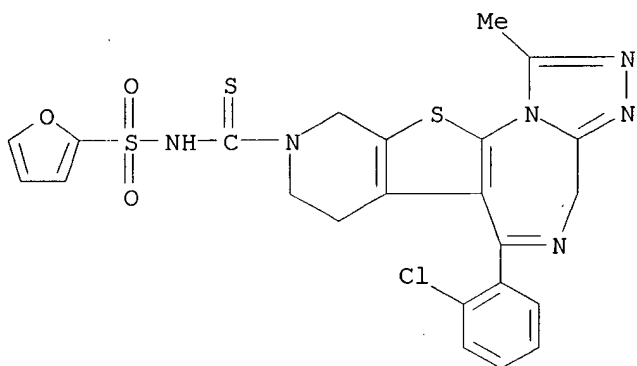


RN 132418-59-8 CAPLUS

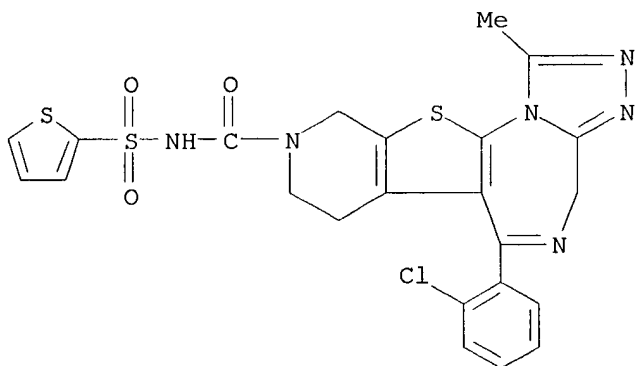
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 132418-60-1 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylsulfonyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



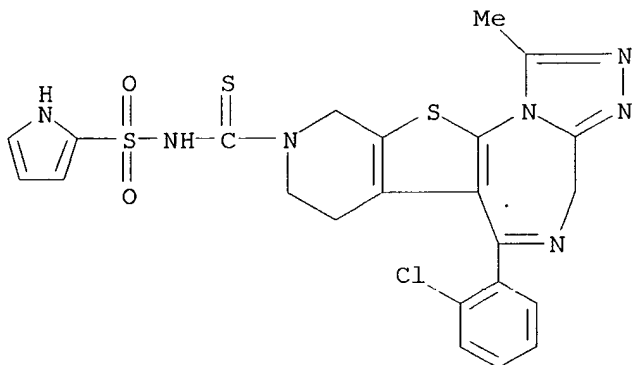
RN 132418-61-2 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



09/701,893

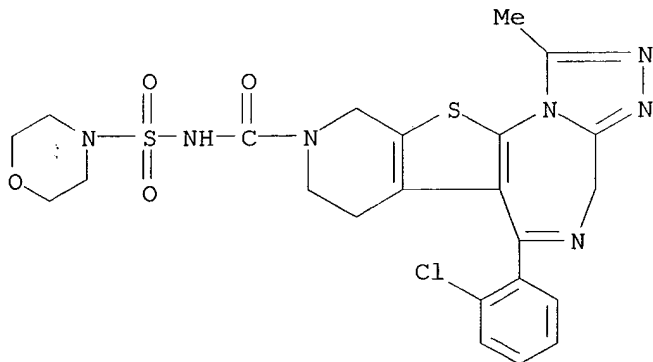
RN 132418-62-3 CAPLUS

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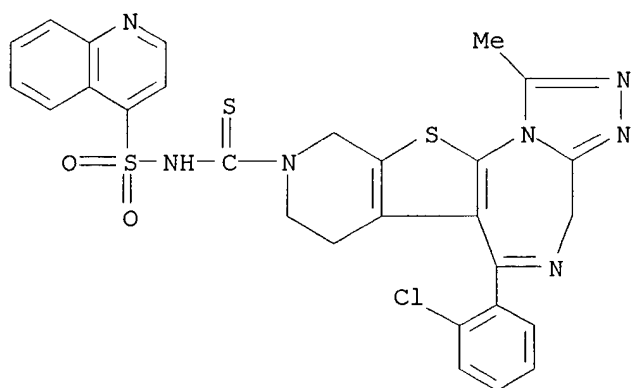
RN 132418-64-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-morpholinylsulfonyl)- (9CI) (CA INDEX NAME)



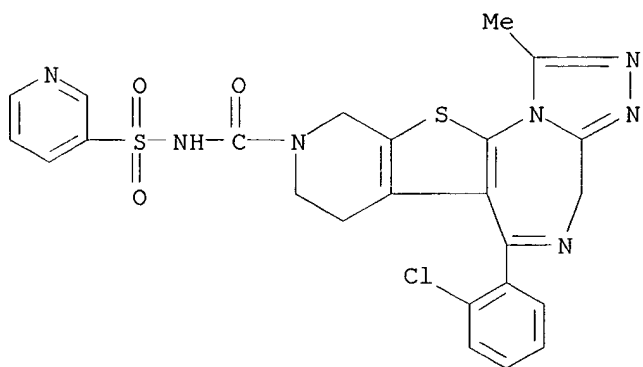
RN 132442-67-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)



RN 138192-67-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 65 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:426595 CAPLUS

DN 117:26595

TI Preparation of thienotriazolodiazepines as benzodiazepine receptor antagonists

IN Braquet, Pierre; Laurent, Jean Pierre; Esanu, Andre; Rolland, Alain

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Fr. Demande, 31 pp.

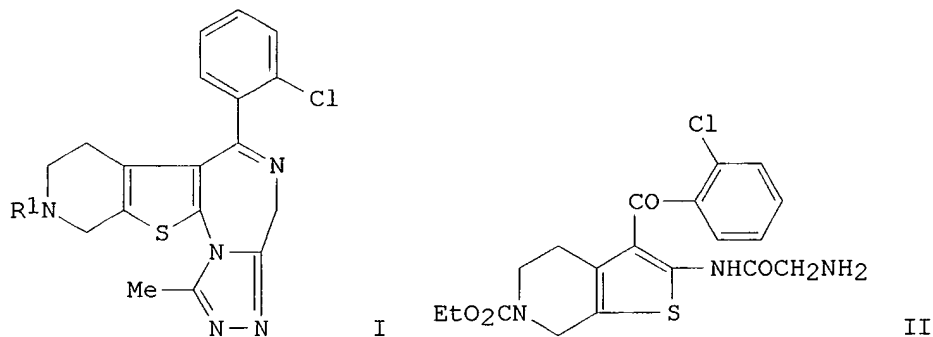
CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2660311	A1	19911004	FR 1990-4159	19900402
	FR 2660311	B1	19940610		
	BE 1003697	A3	19920526	BE 1990-341	19900327
	CH 680366	A	19920814	CH 1990-1045	19900329
	CA 2013516	AA	19910930	CA 1990-2013516	19900330
PRAI	FR 1990-4159		19900402		
OS	MARPAT 117:26595				
GI					



AB Title compds. (I; R1 = RNHC(:Y); R = alkyl, alkenyl, (hetero)aralkyl, substituted Ph, etc.; Y = O, S;] were prepd. Thus, 2-ClC6H4COCH2CN (prepn. given) was cyclocondensed with N-ethoxycarbonyl-4-piperidone and S and the product converted in 2 steps to pyridothiophene II, which was cyclized and the product converted in 5 steps to I [R1 = 4-(MeO)C6H4NHCS]. The latter gave 83.5% inhibition of PAF-induced bronchospasm in monkeys (oral dose not given).

IT 132418-36-1P 132418-37-2P 132418-38-3P
 132418-39-4P 132418-40-7P 132418-41-8P
 132418-42-9P 132418-43-0P 132418-44-1P
 132418-45-2P 132418-46-3P 132418-47-4P
 132418-48-5P 132418-49-6P 132418-50-9P
 132418-51-0P 132418-52-1P 132418-53-2P
 132418-55-4P 132418-56-5P 132418-58-7P
 132418-59-8P 132418-60-1P 132418-61-2P
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 138192-67-3P 139307-99-6P

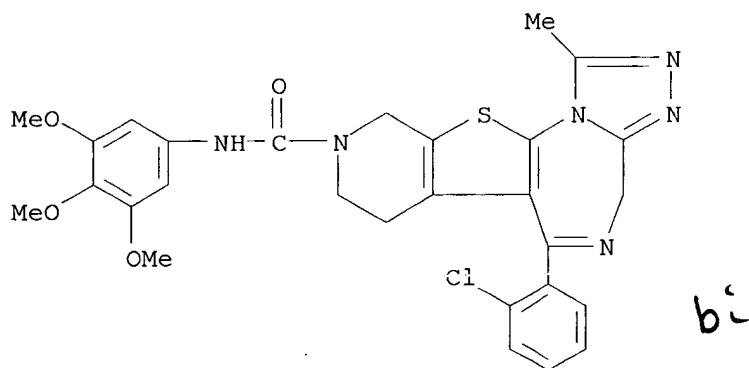
RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as benzodiazepine receptor antagonist)

09/701,893

RN 132418-36-1 CAPLUS

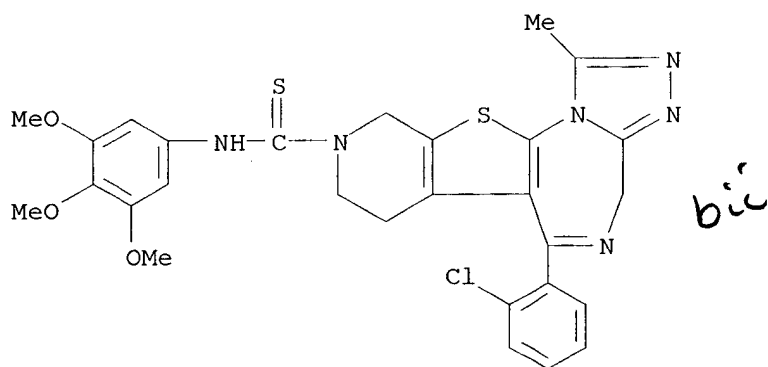
RN 132418-37-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 132418-38-3 CAPLUS

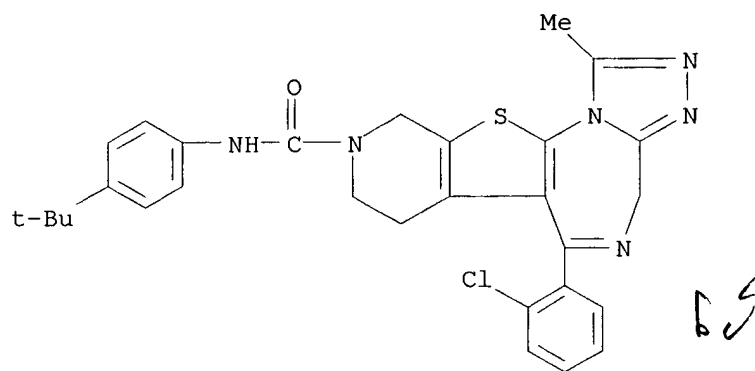
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RN 132418-39-4 CAPLUS

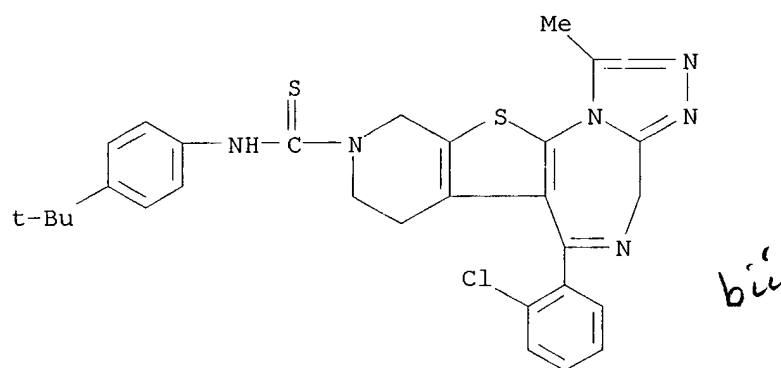
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



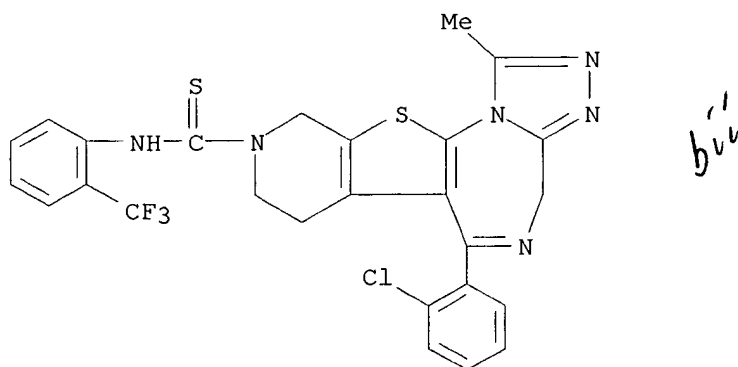
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RN 132418-41-8 CAPLUS

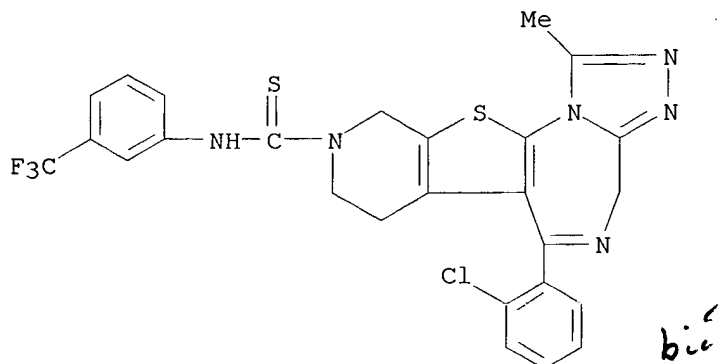
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09/701,893

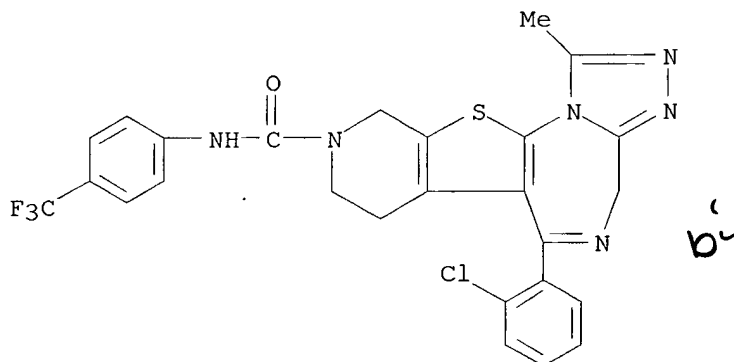
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RN 132418-43-0 CAPLUS

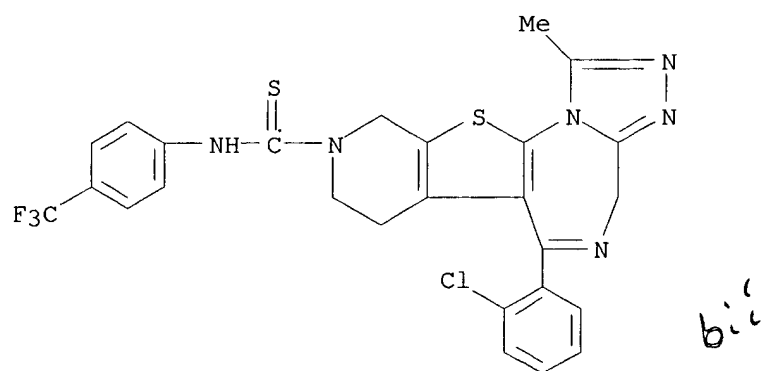
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RN 132418-44-1 CAPLUS

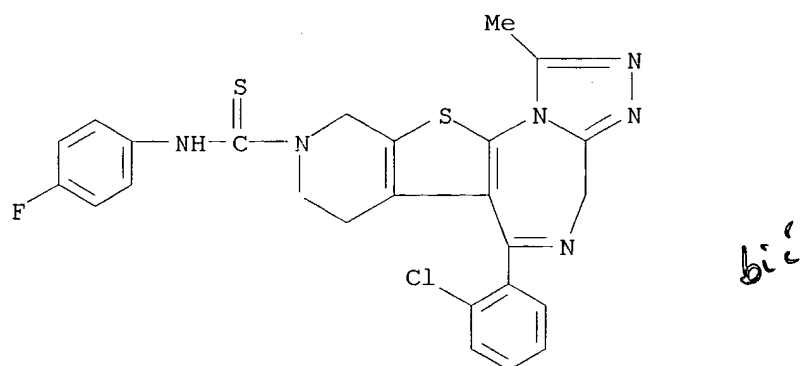
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

09/701,893



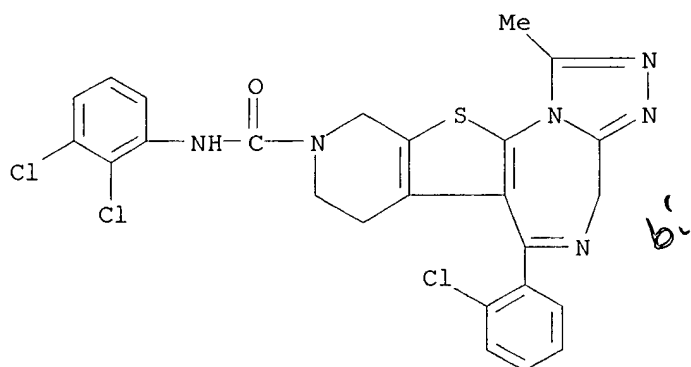
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RN 132418-46-3 CAPLUS

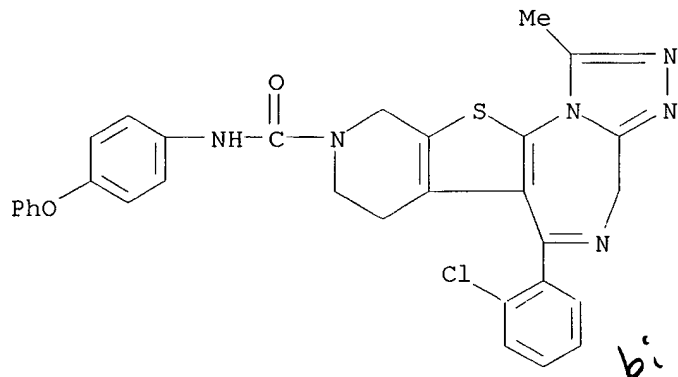
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,3-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

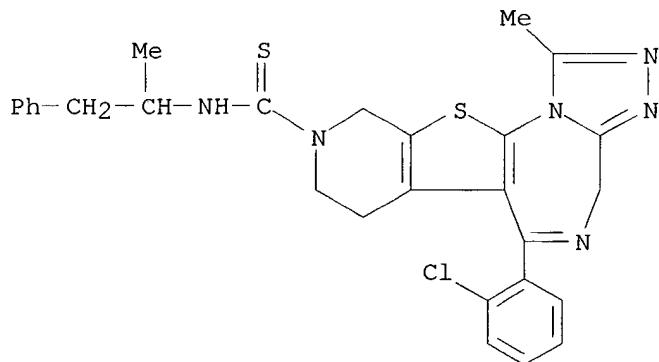
RN 132418-47-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 132418-48-5 CAPLUS

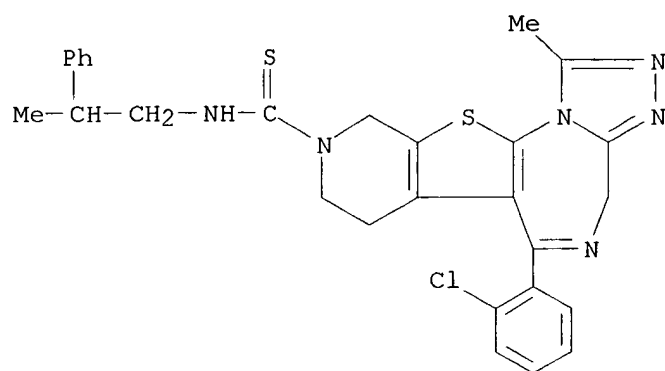
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1-methyl-2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 132418-49-6 CAPLUS

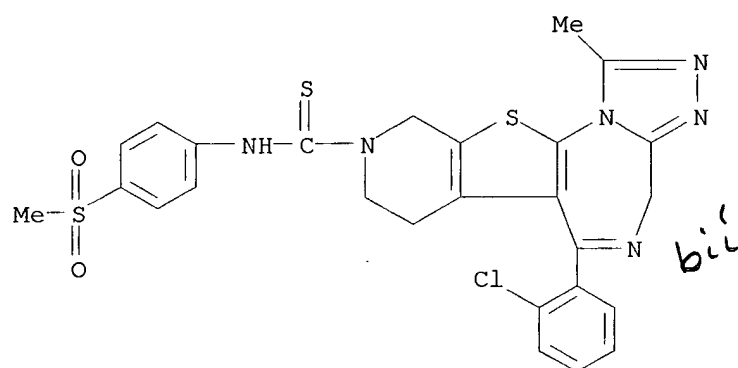
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-phenylpropyl)- (9CI) (CA INDEX NAME)

09/701,893



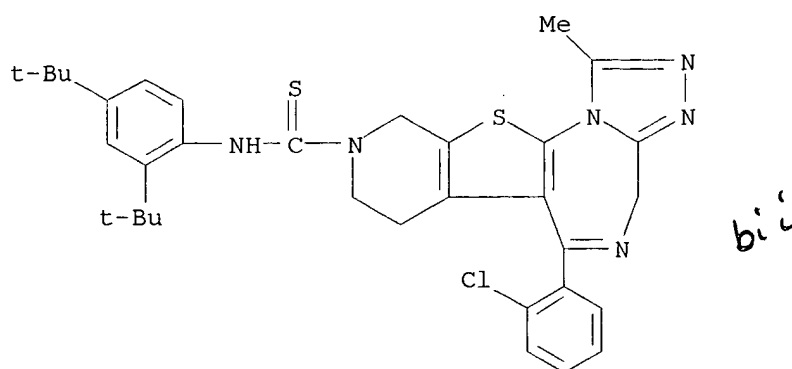
RN 132418-50-9 CAPLUS

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RN 132418-51-0 CAPLUS

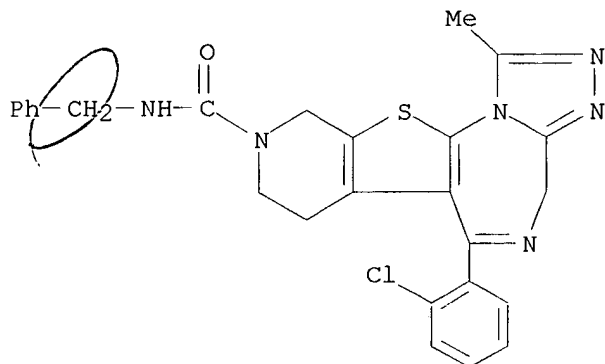
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09/701,893

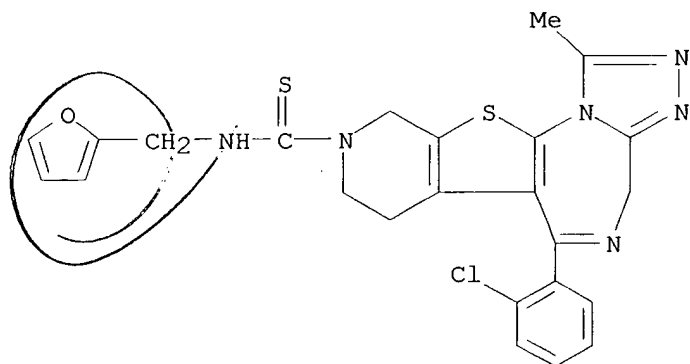
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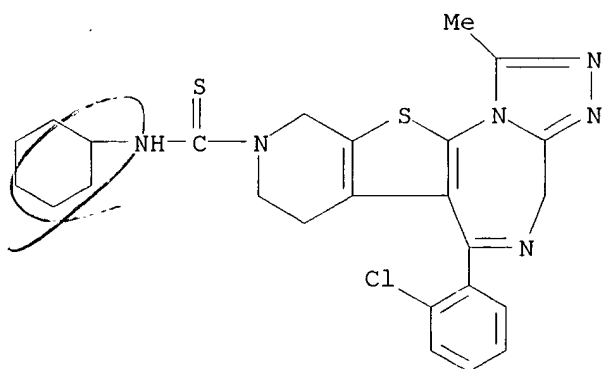
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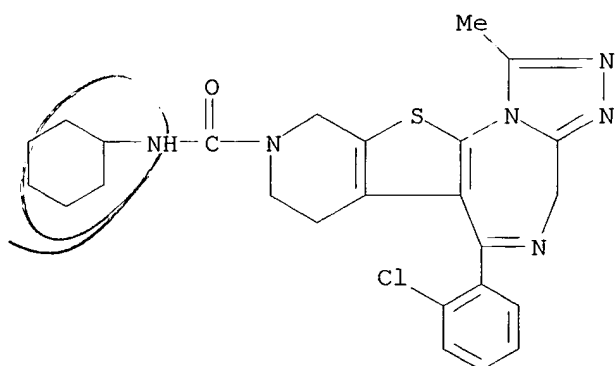
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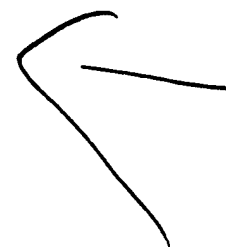
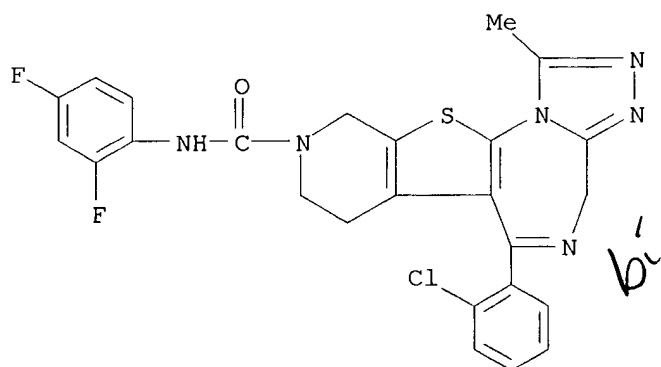
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RN 132418-58-7 CAPLUS

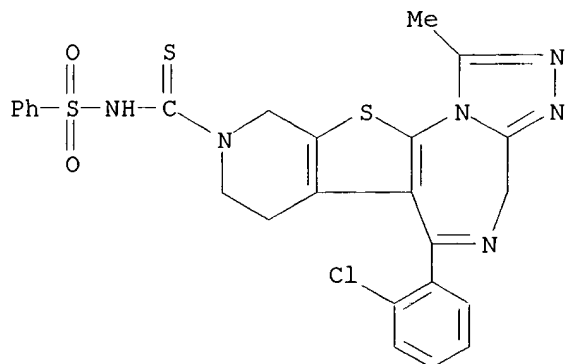
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09/701,893

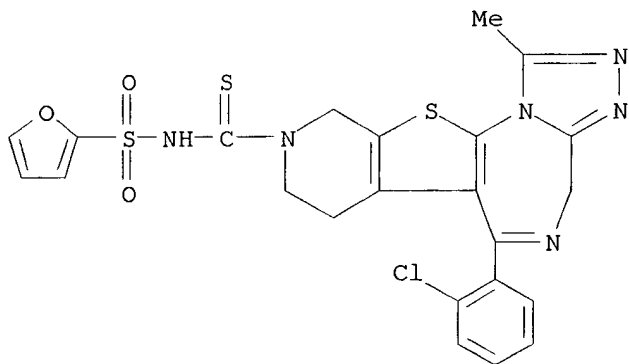
RN 132418-59-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



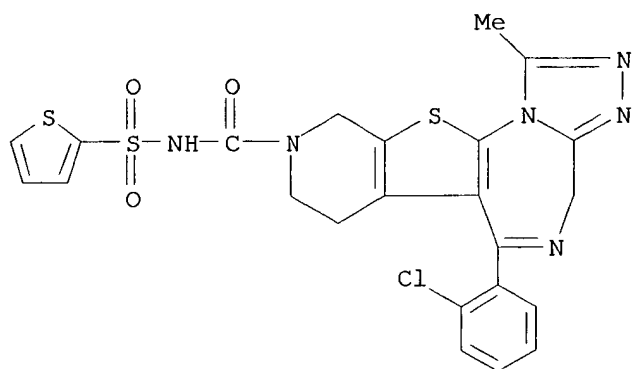
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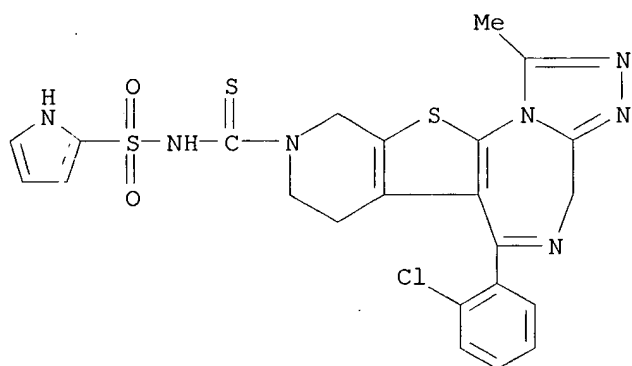


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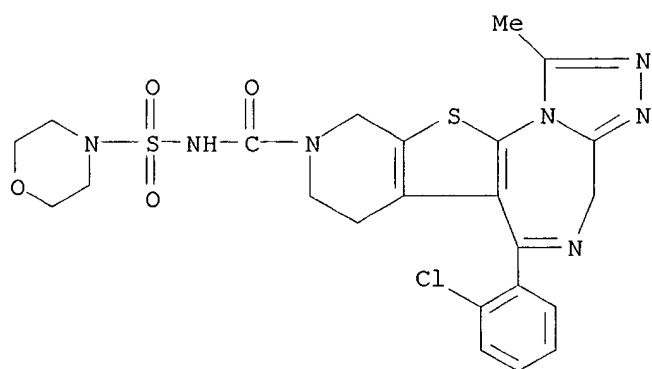
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RN 132418-62-3 CAPLUS
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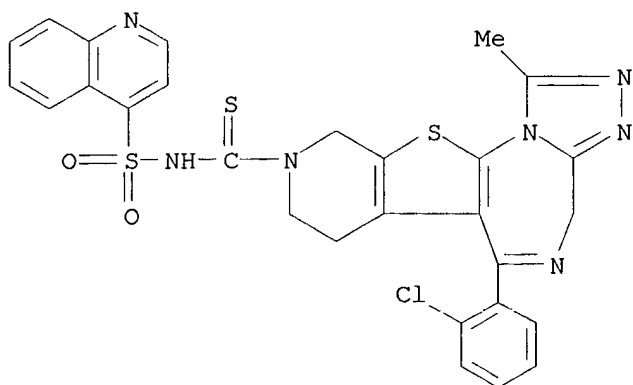
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09/701,893

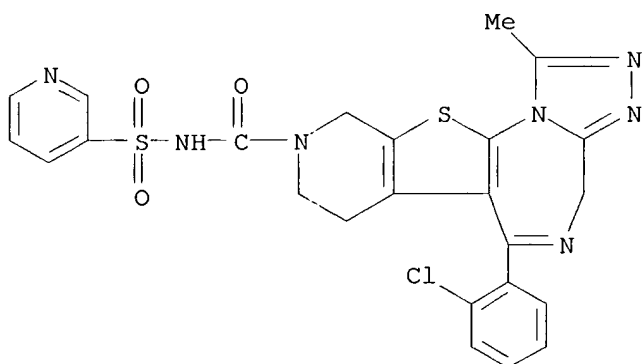
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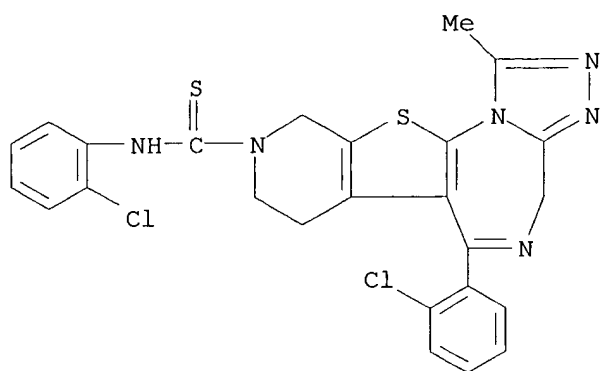
RN 138192-67-3 CAPLUS

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RN 139307-99-6 CAPLUS

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Species
not
in reference

L23 ANSWER 66 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:426550 CAPLUS

DN 117:26550

TI Preparation of pyrido[4',3':4,5]thieno[3,2-f]triazolo[4,3-a]diazepines as platelet activating factor antagonists

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Neth. Appl., 28 pp.

CODEN: NAXXAN

DT Patent

LA Dutch

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	NL 9001090	A	19911202	NL 1990-1090	19900507
OS	MARPAT 117:26550				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I (Y = O or S; R = branched or straight-chain C1-20-alkyl, Ph, Ph substituted with branched or straight-chain C1-5-alkyl, C1-5-alkoxy, halogen, CF₃ or (substituted) phenoxy, furyl, thienyl) are prepd. by reacting amine II at 0-60.degree. with a stoichiometric amt. of RSCH₂CO₂H (R as above) in an aprotic solvent in the presence of a slight stoichiometric excess of dicyclohexylcarbodiimide, reacting the resulting III (R as above) with 3-5 stoichiometric equivs. H₂NNH₂.cntdot.H₂O in a protic solvent at room temp. to 50.degree., and cyclicizing resulting hydrazine IV in a protic solvent with 1-3 equivs. orthoacetate at room temp. to reflux temp. to obtain I (Y = O). Optionally, a sulfuration step is carried out by reacting III with 3-5 stoichiometric equivs. P₂S₅ in an aprotic solvent at at 10.degree. to reflux temp. to obtain I (Y = S). I are nontoxic to mice at doses of 1 g/kg i.p.; their PAF (platelet activating factor)-antagonistic activity that is 10-1000 times higher than that of conventional diazepines, and they are used as antiischemic, antiasthmatic, and antiallergic agents, and as digestive tract-protecting agents.

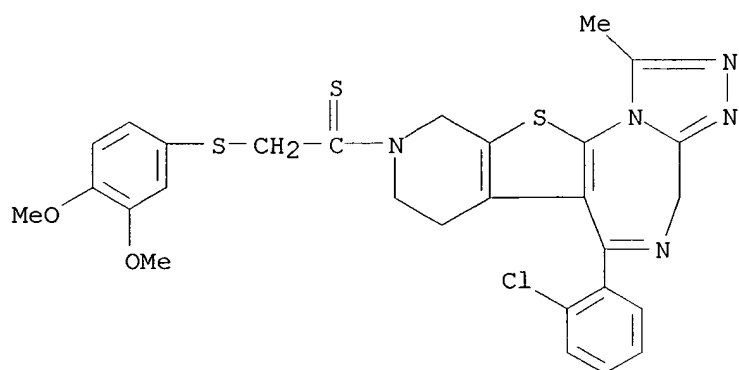
IT 128672-07-1P 132522-27-1P 132522-28-2P
 132522-29-3P 132522-30-6P 132522-31-7P
 132522-32-8P 132522-33-9P 132522-34-0P
 132522-35-1P 132522-36-2P 132522-37-3P
 132522-38-4P 132522-39-5P 132522-40-8P
 132522-42-0P 132522-43-1P 132522-46-4P
 132522-47-5P 132522-48-6P 132522-49-7P
 132522-50-0P 132522-51-1P 132522-52-2P
 132522-53-3P 140383-94-4P 140383-95-5P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as platelet activating factor antagonist)

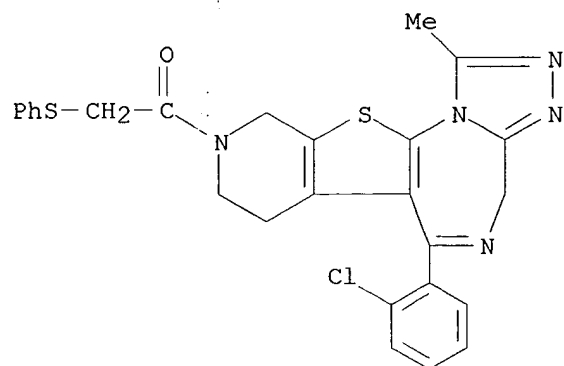
RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



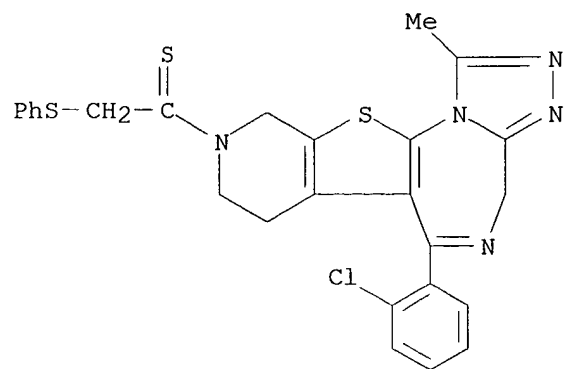
RN 132522-27-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(phenylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-28-2 CAPLUS

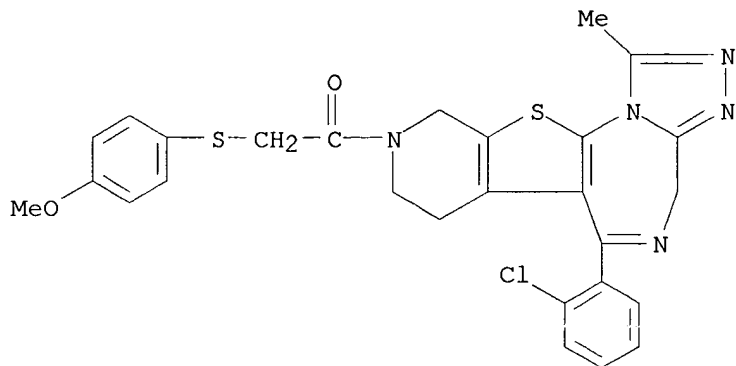
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(phenylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)



RN 132522-29-3 CAPLUS

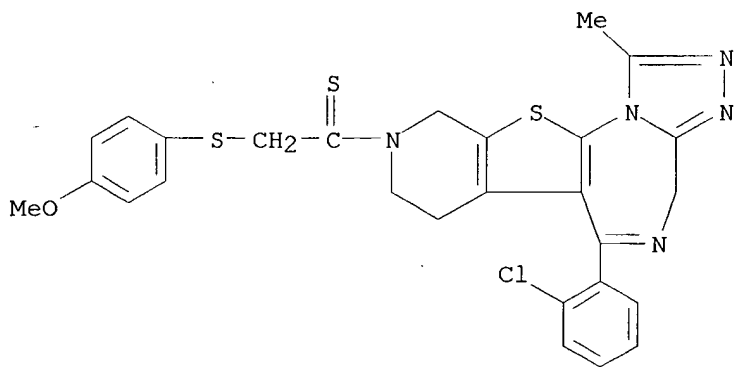
09/701,893

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[[4-methoxyphenylthio]acetyl]-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-30-6 CAPLUS

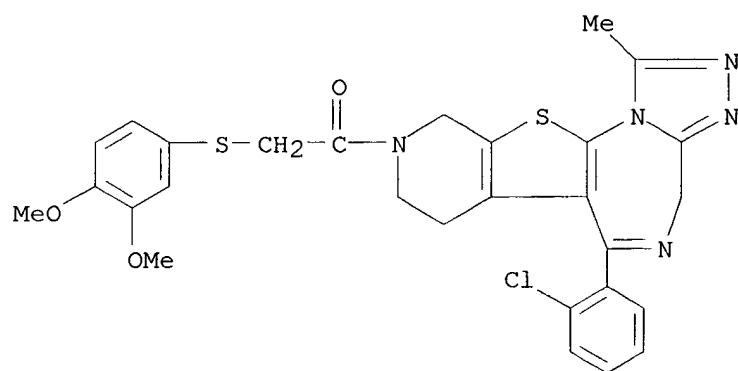
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[2-[(4-methoxyphenyl)thio]-1-
thioxoethyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-31-7 CAPLUS

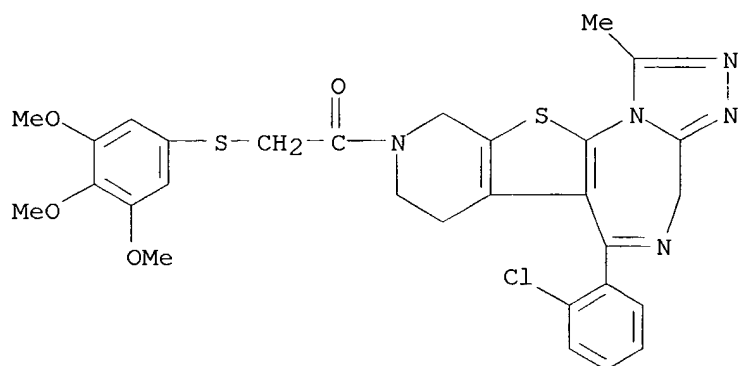
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[3,4-dimethoxyphenylthio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



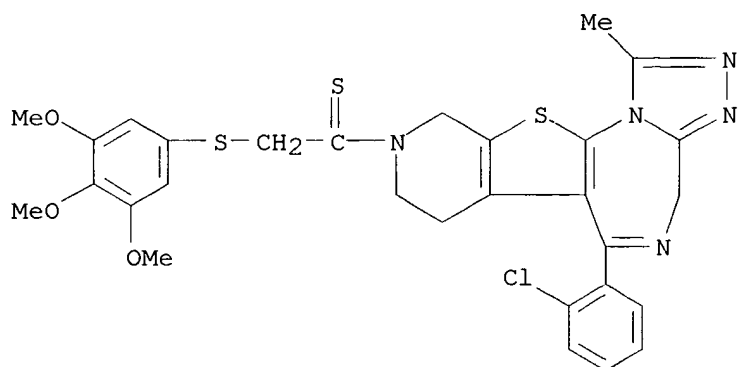
RN 132522-32-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(3,4,5-
trimethoxyphenyl)thio]acetyl- (9CI) (CA INDEX NAME)



RN 132522-33-9 CAPLUS

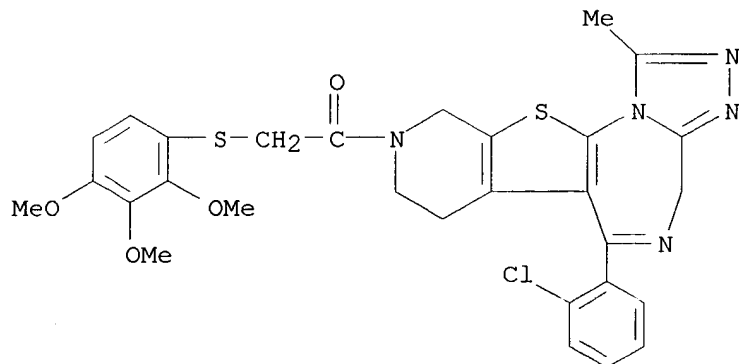
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(3,4,5-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



09/701,893

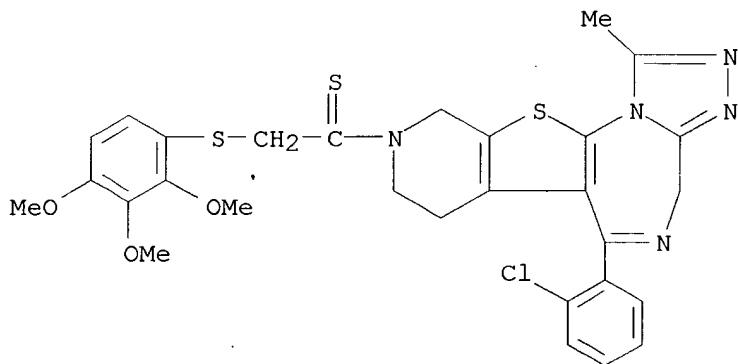
RN 132522-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[2,3,4-
trimethoxyphenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



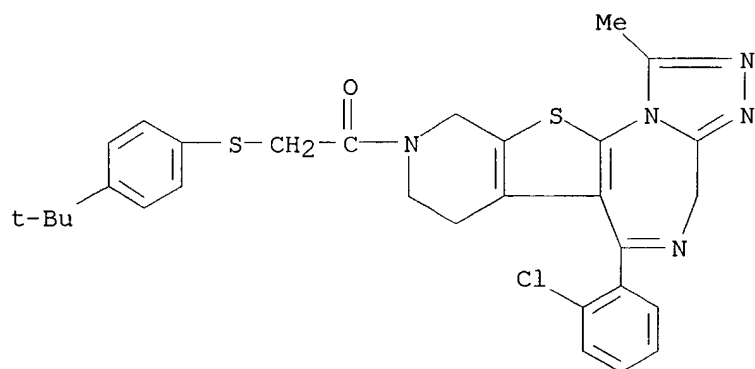
RN 132522-35-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(2,3,4-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



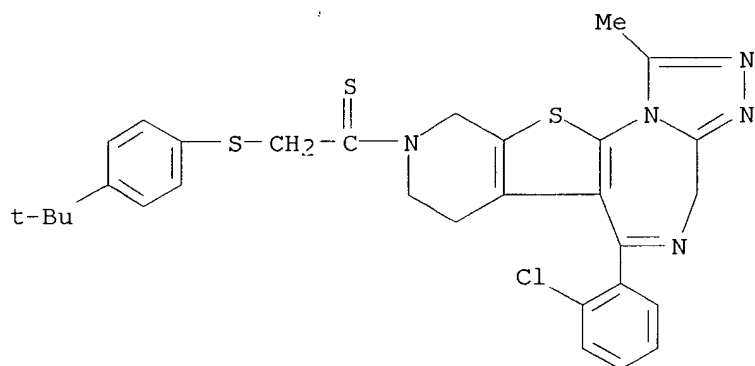
RN 132522-36-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(1,1-dimethylethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



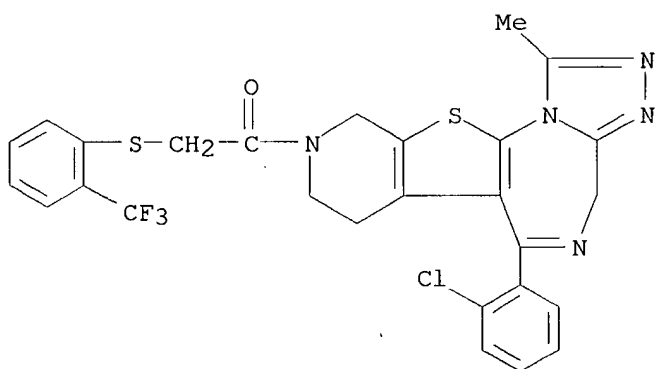
RN 132522-37-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[4-(1,1-dimethylethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-38-4 CAPLUS

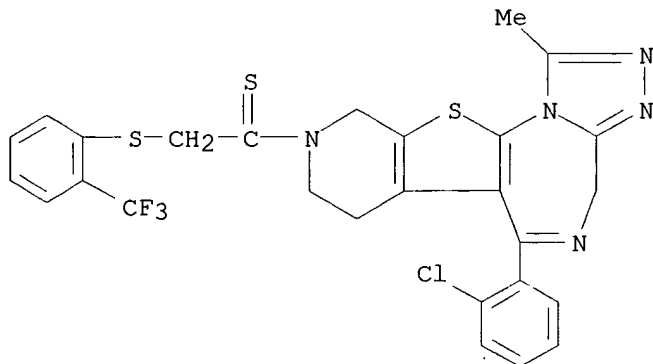
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6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[2-
(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



09/701,893

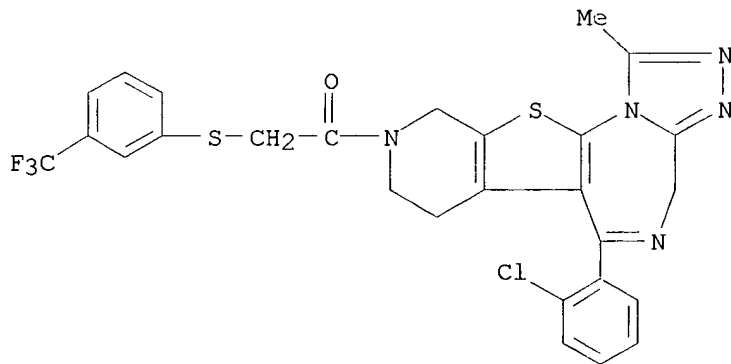
RN 132522-39-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[2-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-40-8 CAPLUS

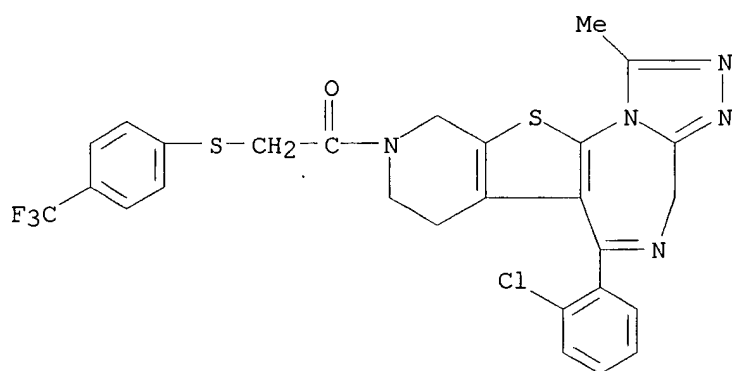
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[3-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-42-0 CAPLUS

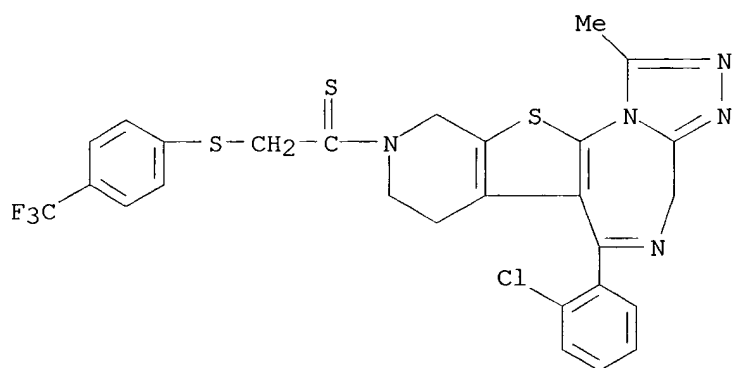
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[4-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)

09/701,893



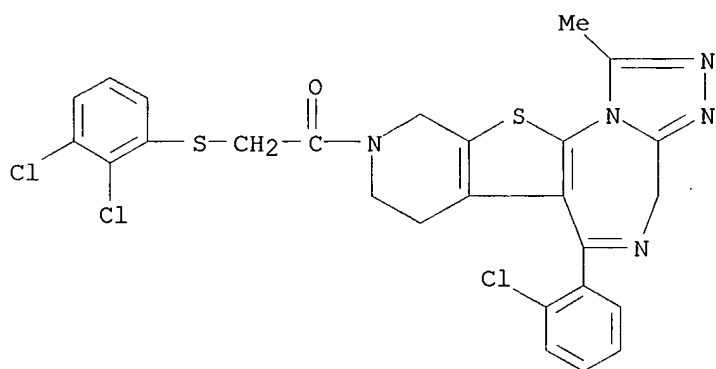
RN 132522-43-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[4-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-46-4 CAPLUS

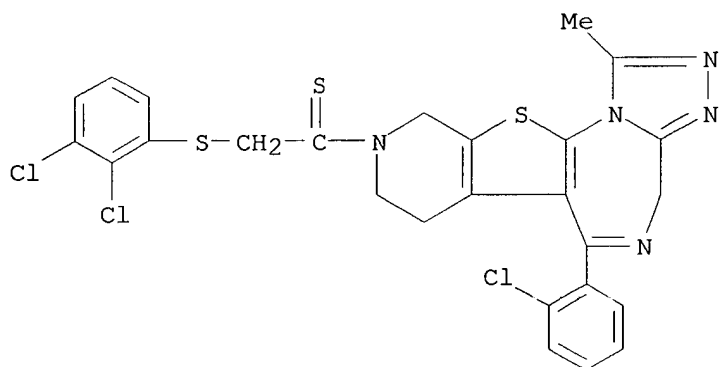
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[2,3-dichlorophenyl]thio]acetyl-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

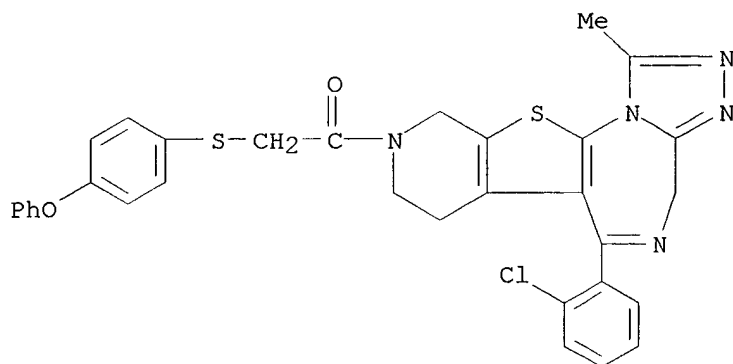
RN 132522-47-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(2,3-dichlorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-48-6 CAPLUS

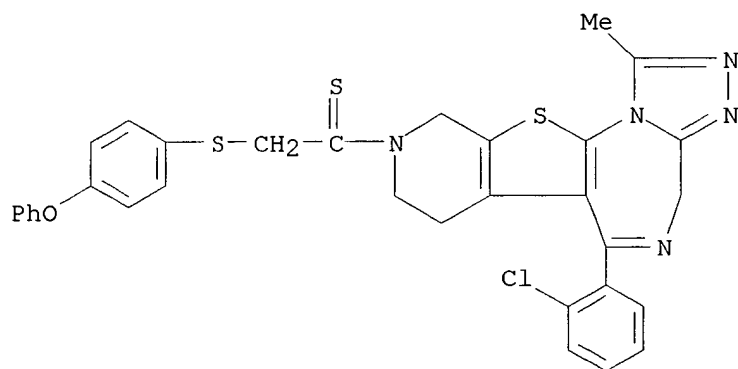
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[4-
phenoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-49-7 CAPLUS

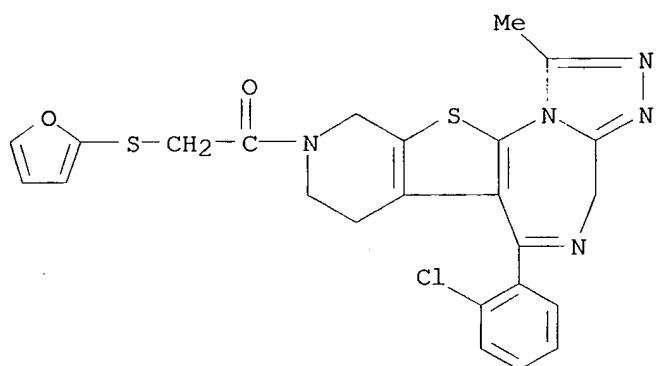
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-[(4-
phenoxyphenyl)thio]-1-thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893



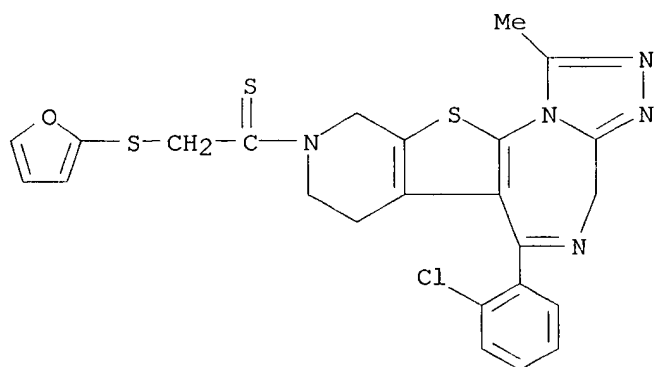
RN 132522-50-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(2-furanylthio)acetyl]-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



RN 132522-51-1 CAPLUS

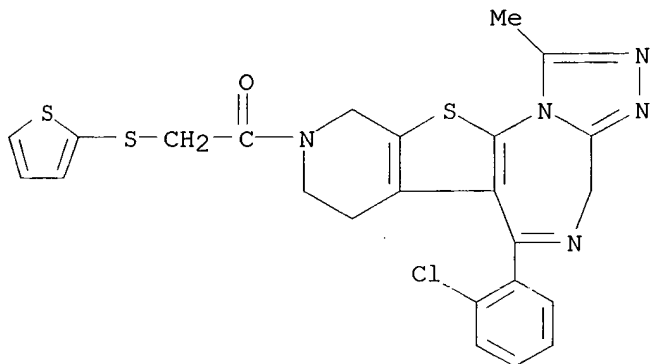
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-(2-furanylthio)-1-thioxoethyl]-7,8,9,10-tetrahydro-
1-methyl- (9CI) (CA INDEX NAME)



09/701,893

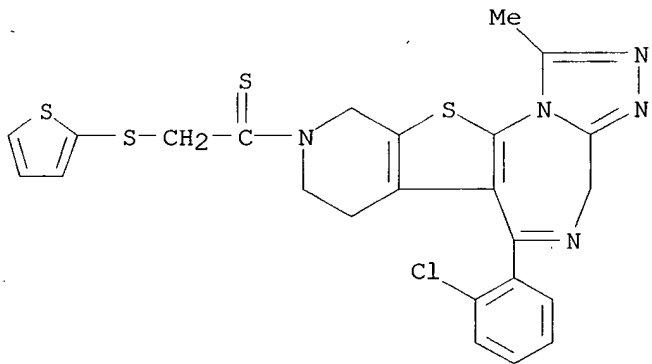
RN 132522-52-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-thienylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-53-3 CAPLUS

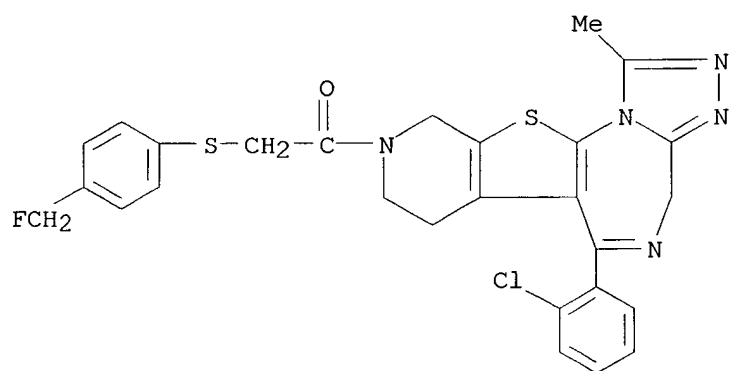
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-thienylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)



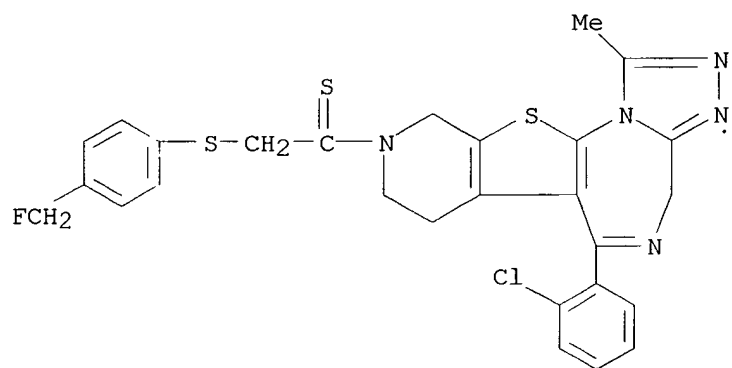
RN 140383-94-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(fluoromethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 140383-95-5 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[4-(fluoromethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 67 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:426525 CAPLUS

DN 117:26525

TI Hapten synthesis for (+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f]triazolo[4,3-a][1,4]diazepine (E6123)

AU Miyazawa, Shuhei; Okano, Kazuo; Kawahara, Tetsuya; Machida, Yoshimasa; Yamatsu, Isao

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

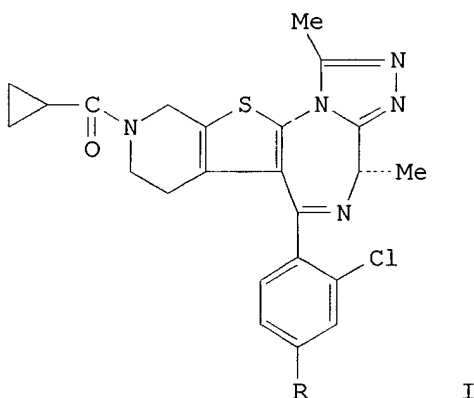
SO Chem. Pharm. Bull. (1992), 40(3), 762-5

CODEN: CPBTAL; ISSN: 0009-2363

DT Journal

LA English

GI



AB In order to examine the pharmacokinetics of E6123 (I; R = H) at low doses, establishment of a RIA is required. On the basis of the metabolic pattern of I (R = H), the potential hapten I (R = CH₂CH₂CO₂H) was synthesized. For the synthesis, the butynyloxycarbonyl group was developed as a piperidine N-protective group to prevent oxidn. of the methylene at position 2. This protecting group is stable under usual basic and acidic conditions.

IT **131614-02-3**, E6123

RL: RCT (Reactant)

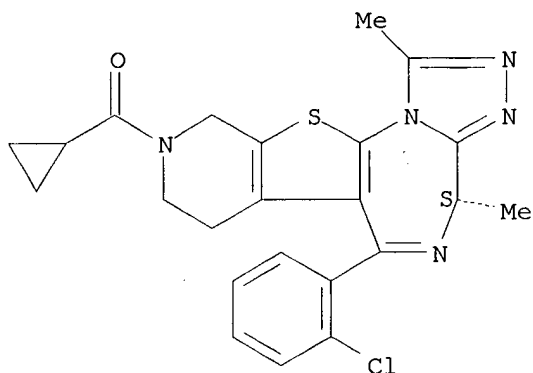
(hapten for, prepn. of)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



IT **130311-76-1**

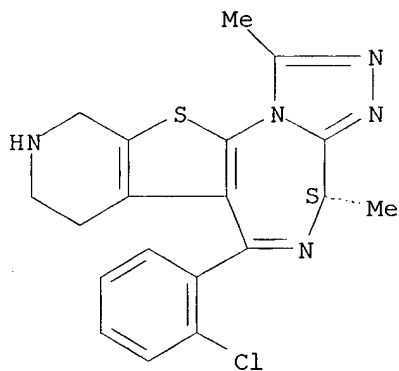
RL: RCT (Reactant)

(oxidn. of, with manganese dioxide)

RN 130311-76-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



9



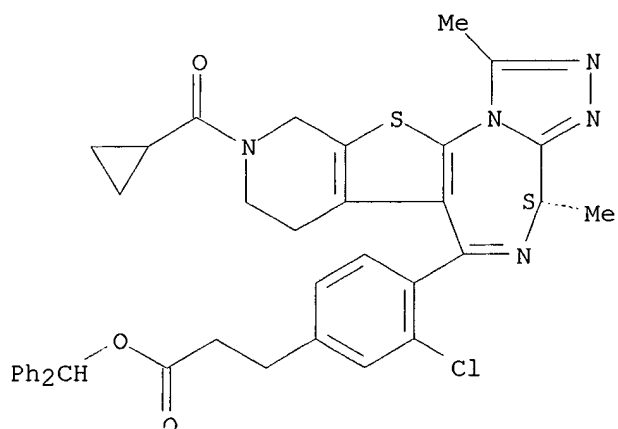
IT **141783-08-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ester hydrolysis of)

RN 141783-08-6 CAPLUS

CN Benzenepropanoic acid, 3-chloro-4-[9-(cyclopropylcarbonyl)-7,8,9,10-
tetrahydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-
f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl]-, diphenylmethyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

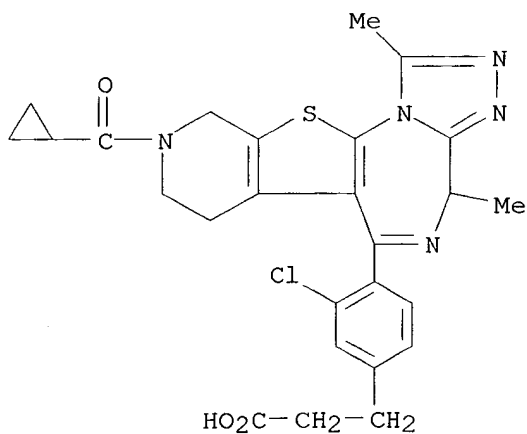


IT **141733-87-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of)

RN 141733-87-1 CAPLUS

CN Benzenepropanoic acid, 3-chloro-4-[9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl]- (9CI) (CA INDEX NAME)

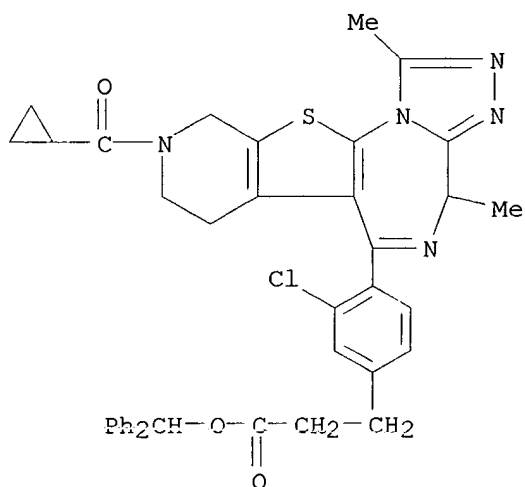


IT **141733-88-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resoln. of)

RN 141733-88-2 CAPLUS

CN Benzenepropanoic acid, 3-chloro-4-[9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl]-, diphenylmethyl ester (9CI)
(CA INDEX NAME)



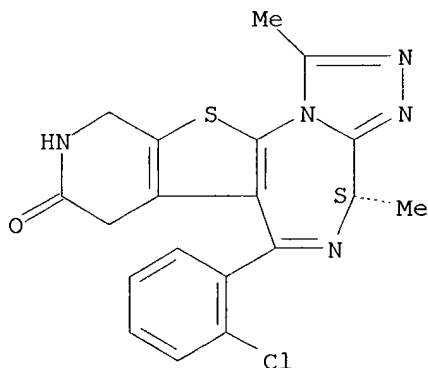
IT 141733-89-3P 141783-07-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 141733-89-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-8(7H)-one, 6-(2-chlorophenyl)-9,10-dihydro-1,4-dimethyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 141783-07-5 CAPLUS

CN Benzenepropanoic acid, 3-chloro-4-[9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L23 ANSWER 68 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:235664 CAPLUS

DN 116:235664

TI Preparation of pyrido[4',3',4:5]thieno[3,2-f]triazolo[4,3-a]diazepines as drugs

IN Braquet, Pierre; Laurent, Jean Pierre; Esanu, Andre; Pommier, Jacques

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Fr. Demande, 34 pp.

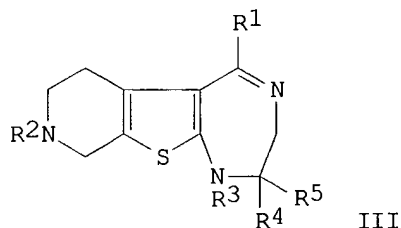
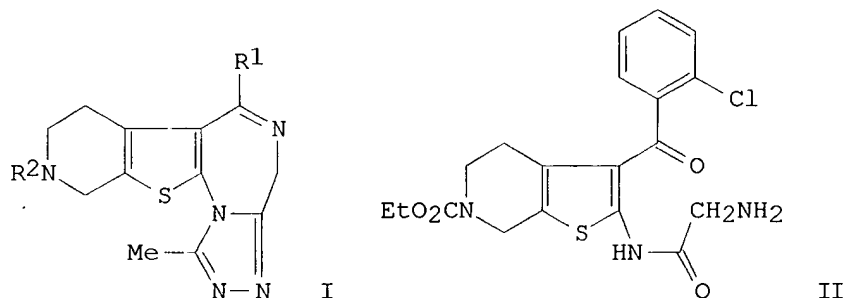
CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2661911	A1	19911115	FR 1990-5882	19900511
	FR 2661911	B1	19920731		
	CH 681010	A	19921231	CH 1990-1521	19900504
PRAI	FR 1990-5882		19900511		
OS	MARPAT 116:235664				
GI					



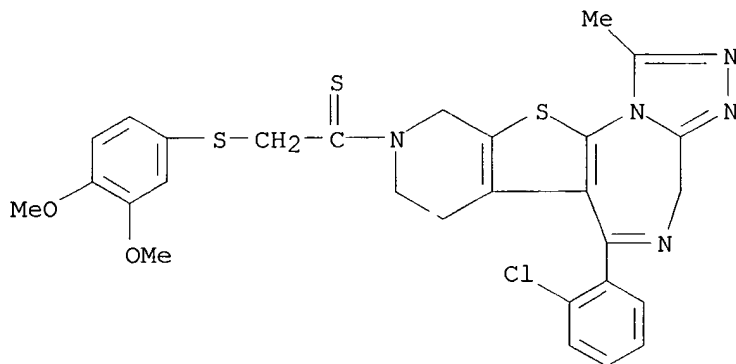
AB Title compds. [I; R1 = 2-ClC6H4; R2 = C(:Y)CH2SR; R = alkyl, furyl, thienyl, (substituted) Ph; Y = O, S] were prepd. as PAF and benzodiazepine receptor antagonists. Thus, 2-ClC6H4COCH2CN (prepn. given) was cyclocondensed with N-ethoxycarbonyl-4-piperidone and S and the product converted in 2 steps to tetrahydropyridothienodiazepine II which was cyclized and the product deprotected to give pyrido[4',3',4:5]thieno[3,2-f]triazolo[4,3-a]diazepine III (R1 = 2-ClC6H4, R2 = R3 = H, R4R5 = O). The latter was converted in 2 steps to III (R1 unchanged, R2 COCH2SCHMe2, R3R4 = bond, R5 = NHNH2) which was cyclocondensed with MeC(OEt)3 to give I (R1 = 2-ClC6H4, R2 = COCH2SCHMe2) which gave 54.2% protection against induced hippocampal ischemia in gerbils at 10 mg/kg (route of administration not given).

IT 128672-07-1P 132522-27-1P 132522-28-2P
 132522-29-3P 132522-30-6P 132522-31-7P
 132522-32-8P 132522-33-9P 132522-34-0P
 132522-35-1P 132522-36-2P 132522-37-3P
 132522-38-4P 132522-39-5P 132522-40-8P
 132522-41-9P 132522-42-0P 132522-43-1P
 132522-44-2P 132522-45-3P 132522-46-4P
 132522-47-5P 132522-48-6P 132522-49-7P
 132522-50-0P 132522-51-1P 132522-52-2P
 132522-53-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as PAF and benzodiazepine receptor antagonist)

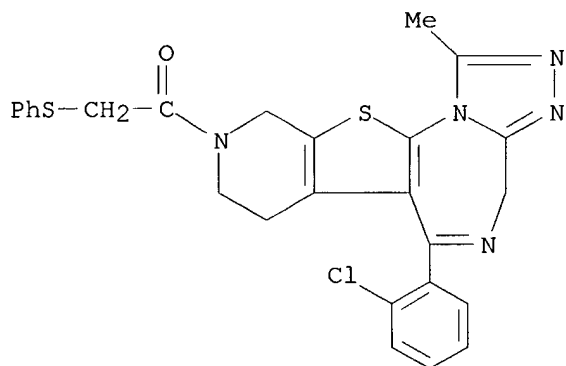
RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-
 7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



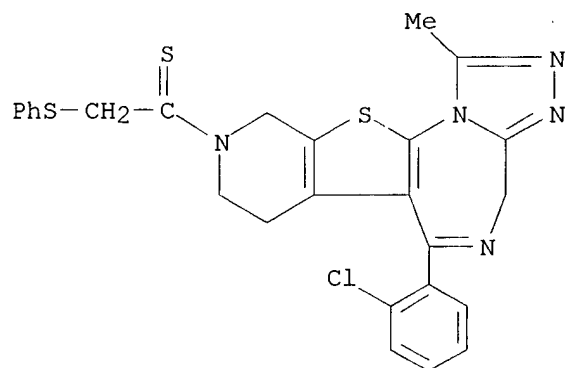
RN 132522-27-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(phenylthio)acetyl]-
 (9CI) (CA INDEX NAME)



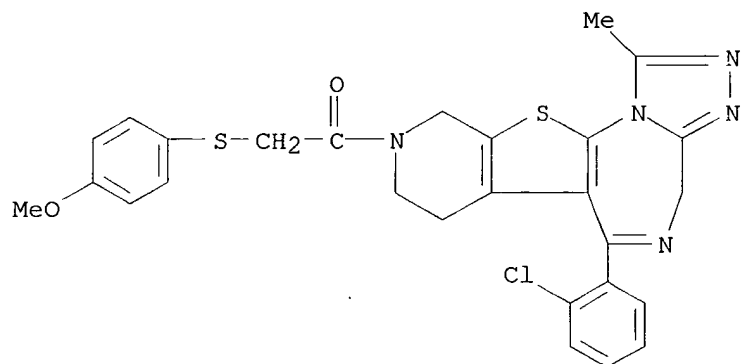
RN 132522-28-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(phenylthio)-1-
 thioxoethyl]- (9CI) (CA INDEX NAME)



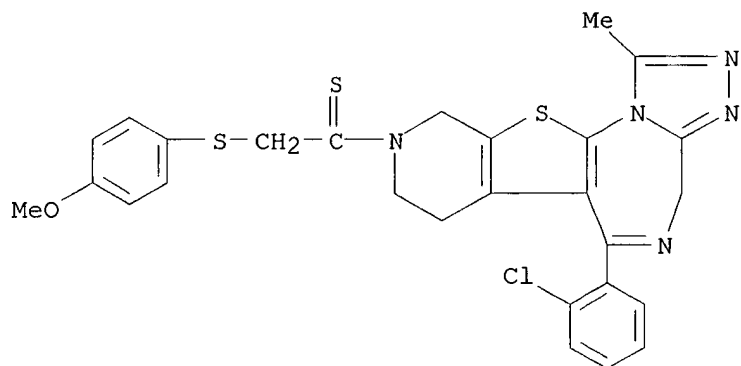
RN 132522-29-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(4-methoxyphenyl)thio]acetyl-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-30-6 CAPLUS

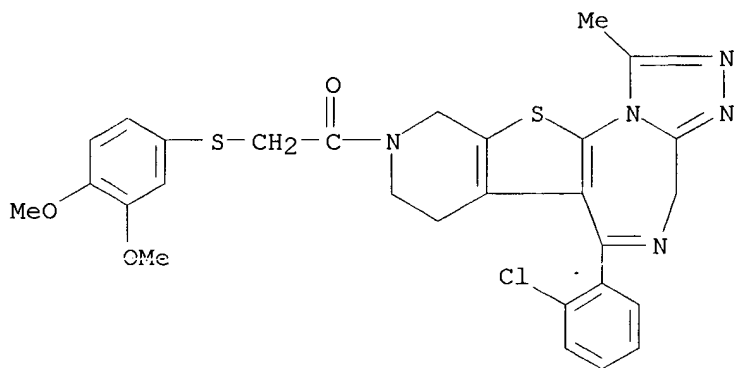
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[2-[(4-methoxyphenyl)thio]-1-
thioxoethyl]-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

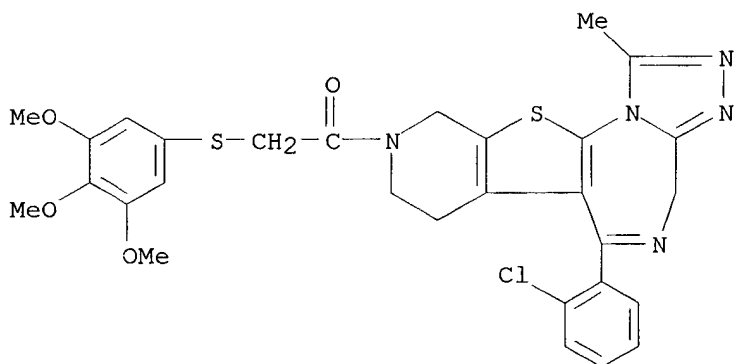
RN 132522-31-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[(3,4-dimethoxyphenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-32-8 CAPLUS

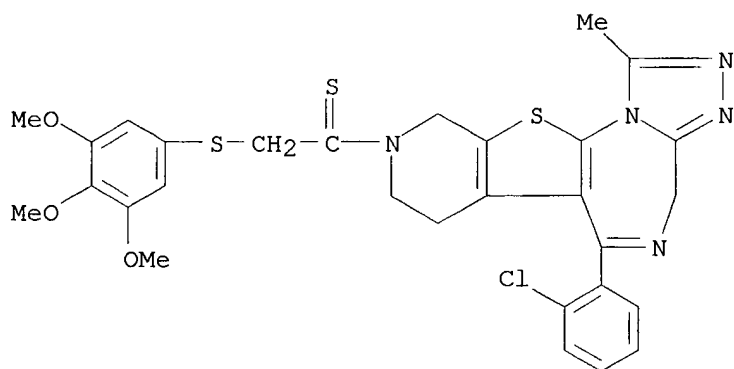
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(3,4,5-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-33-9 CAPLUS

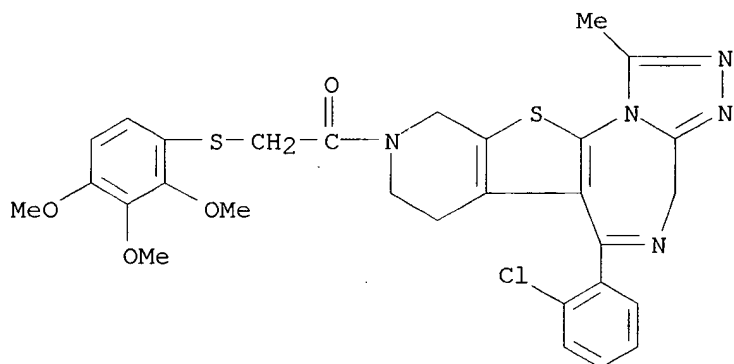
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(3,4,5-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)

09/701,893



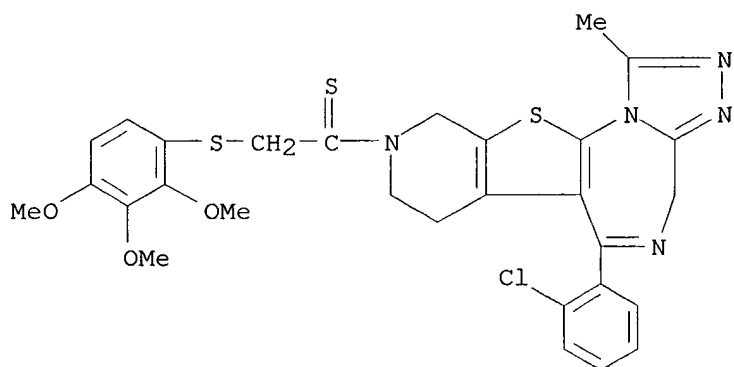
RN 132522-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(2,3,4-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-35-1 CAPLUS

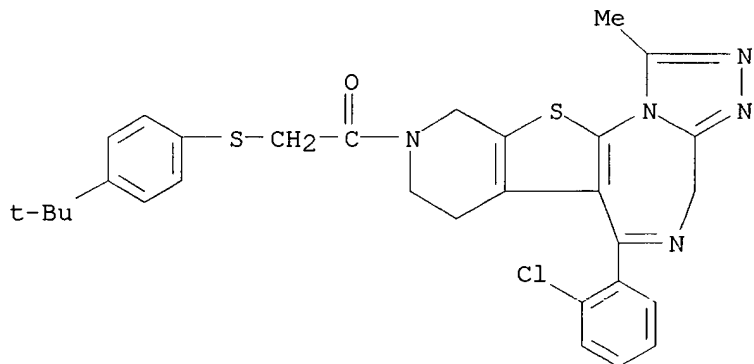
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(2,3,4-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



09/701,893

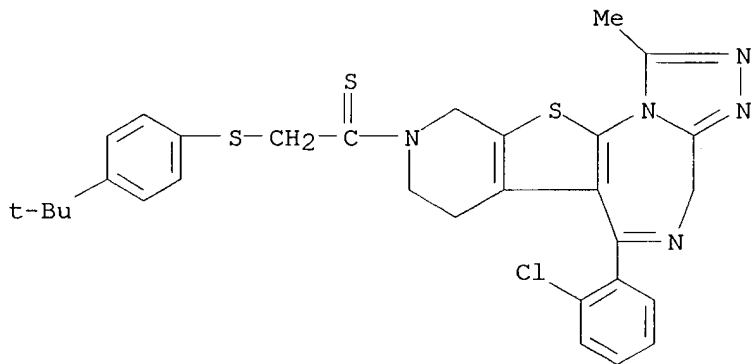
RN 132522-36-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(1,1-dimethylethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



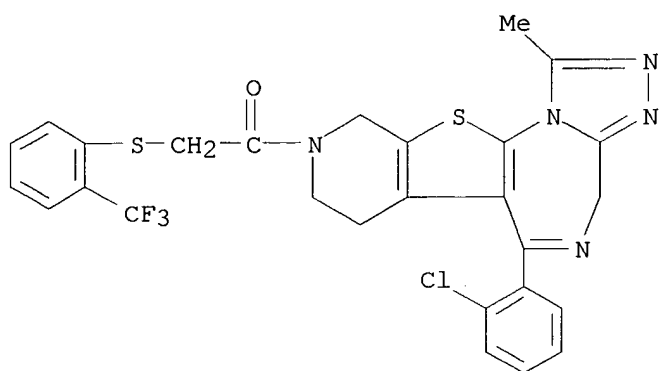
RN 132522-37-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[[4-(1,1-dimethylethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



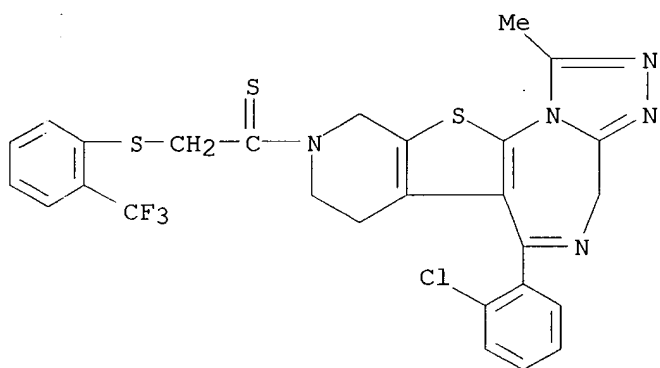
RN 132522-38-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[2-
(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



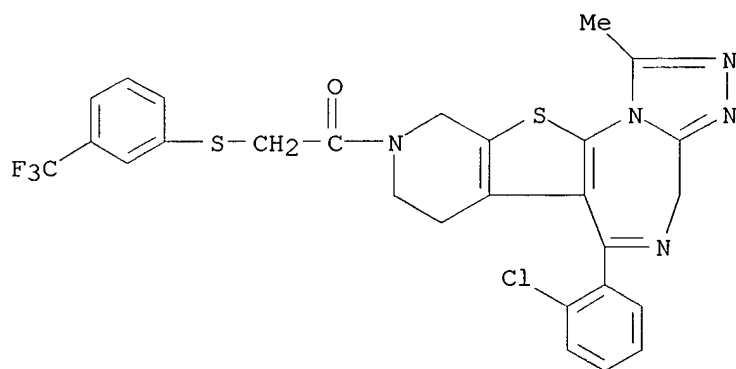
RN 132522-39-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[1-thioxo-2-[[2-
(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-40-8 CAPLUS

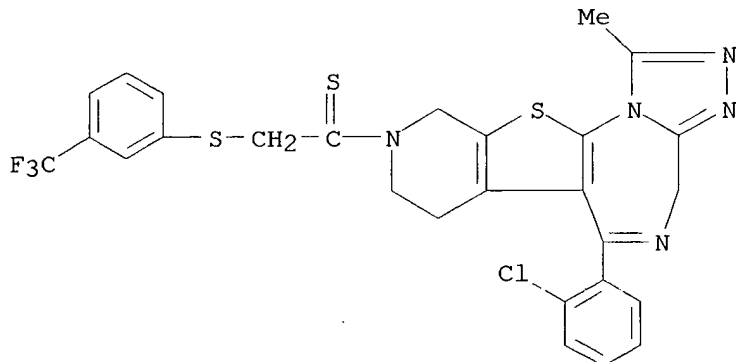
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[3-
(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



09/701,893

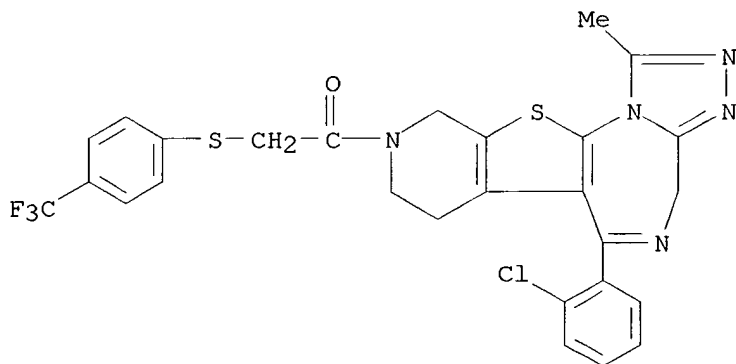
RN 132522-41-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[3-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-42-0 CAPLUS

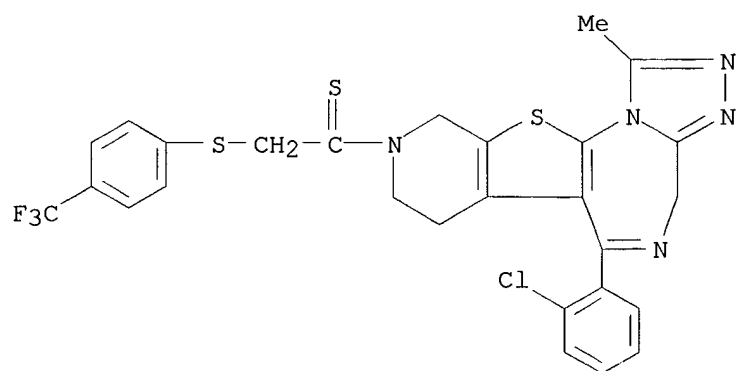
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[4-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-43-1 CAPLUS

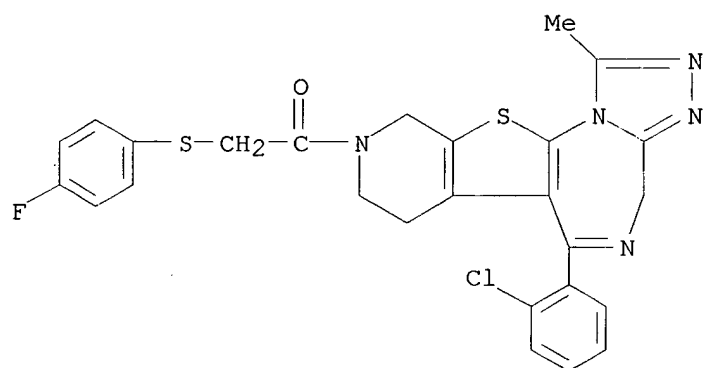
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[4-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)

09/701,893



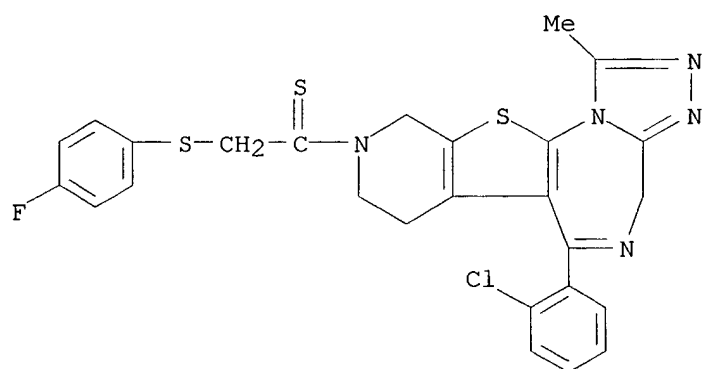
RN 132522-44-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(4-fluorophenyl)thio]acetyl-7,8,9,10-tetrahydro-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-45-3 CAPLUS

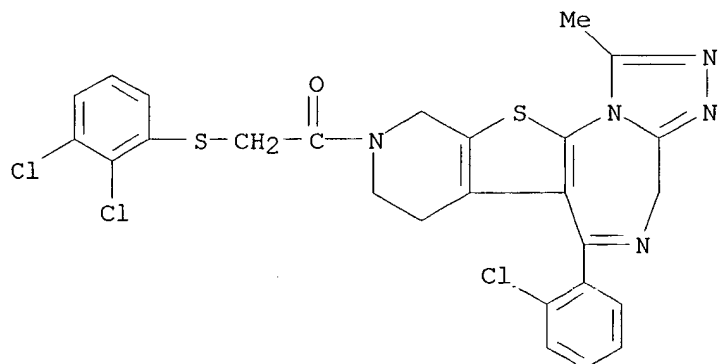
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(4-fluorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

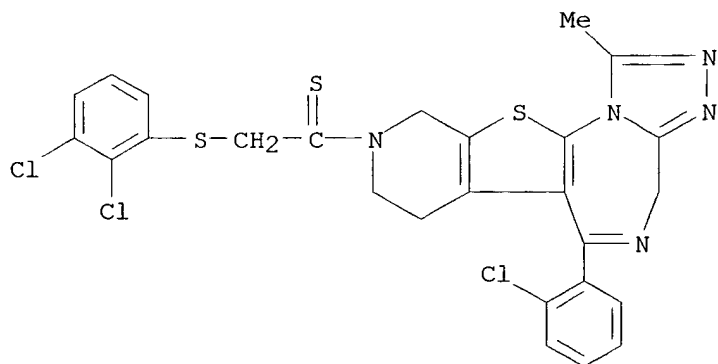
RN 132522-46-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[(2,3-dichlorophenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-47-5 CAPLUS

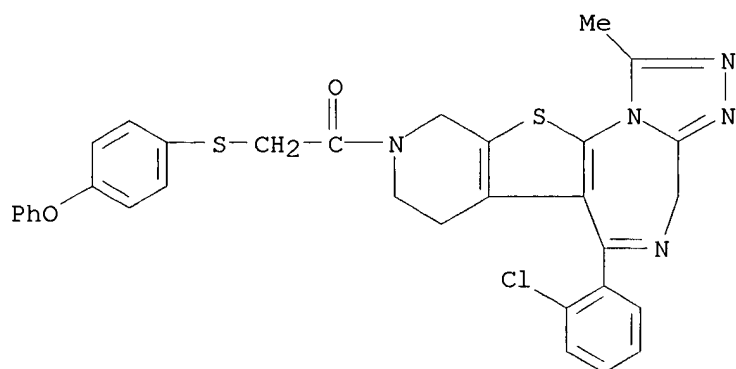
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(2,3-dichlorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-48-6 CAPLUS

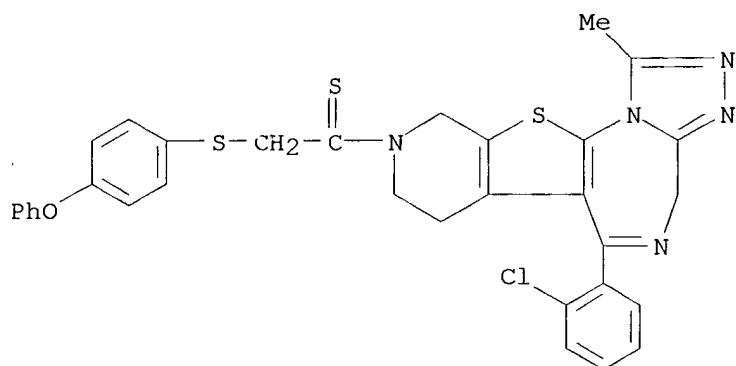
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(4-
phenoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)

09/701,893



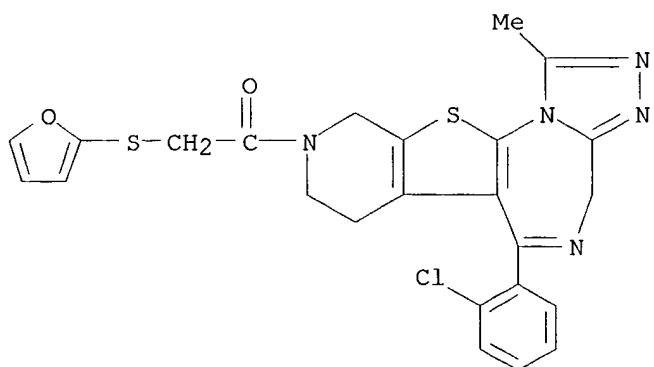
RN 132522-49-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-[(4-
phenoxyphenyl)thio]-1-thioxoethyl]- (9CI) (CA INDEX NAME)



RN 132522-50-0 CAPLUS

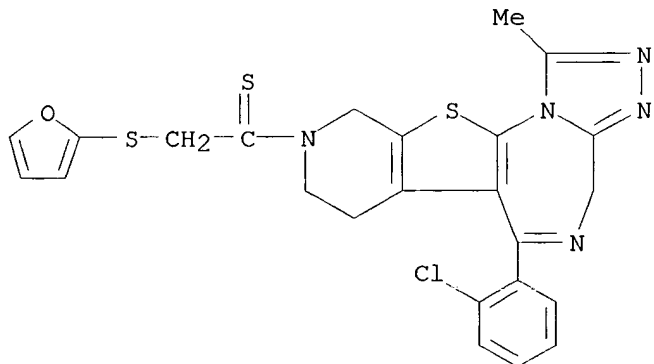
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(2-furanylthio)acetyl]-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



09/701,893

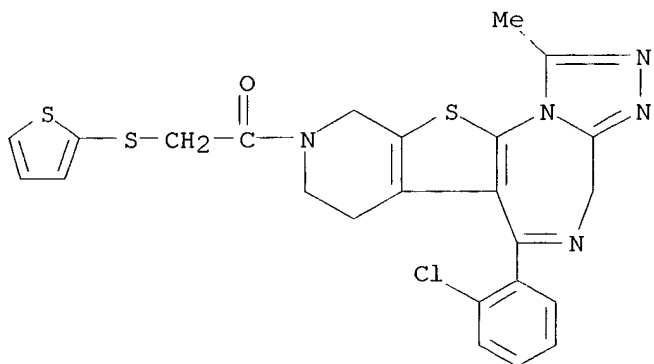
RN 132522-51-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-(2-furanylthio)-1-thioxoethyl]-7,8,9,10-tetrahydro-
1-methyl- (9CI) (CA INDEX NAME)



RN 132522-52-2 CAPLUS

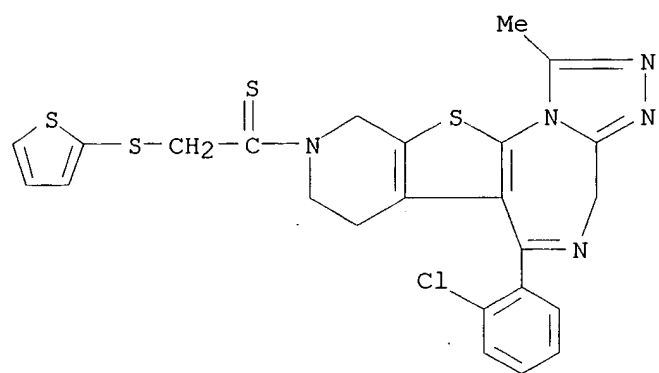
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-thienylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-53-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-thienylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 69 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:235592 CAPLUS

DN 116:235592

TI A practical synthesis of optically active platelet-activating factor antagonist, (+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (E6123), and its absolute configuration

AU Miyazawa, Shuhei; Okano, Kazuo; Shimomura, Naoyuki; Kawahara, Tetsuya; Asano, Osamu; Yoshimura, Hiroyuki; Kawai, Takatoshi; Souda, Shigeru; Yoshida, Yutaka; et al.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

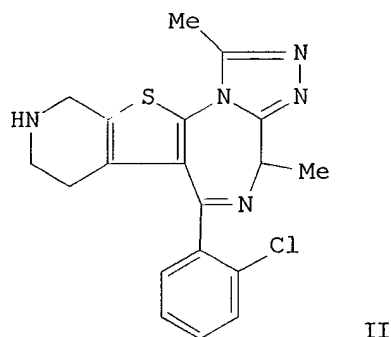
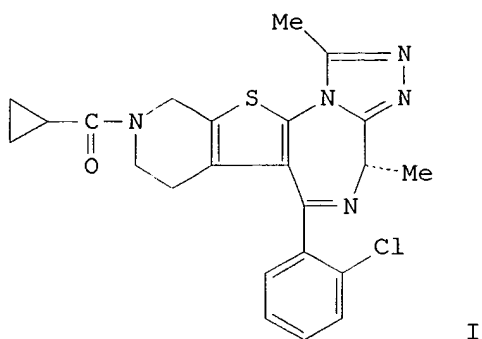
SO Chem. Pharm. Bull. (1992), 40(2), 521-3

CODEN: CPBTAL; ISSN: 0009-2363

DT Journal

LA English

GI



AB The title compd. I was prepd. on a large scale by the optical resolu. of racemic pyridothienotriazolodiazepine II using (+)-dibenzoyl-D-tartaric acid to get (-)-II, followed by N-acylation with cyclopropanecarbonyl chloride. X-ray crystallog. anal. of I indicated that the abs. configuration of (+)-I was S.

IT **141085-66-7**

RL: PRP (Properties)
(crystal structure of)

RN 141085-66-7 CAPLUS

CN Ethanol, compd. with (S)-6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-

09/701,893

7,8,9,10-tetrahydro-1,4-dimethyl-4H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (1:2) (9CI) (CA INDEX NAME)

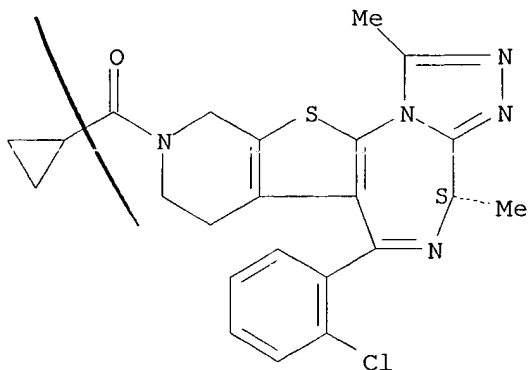
CM 1

CRN 131614-02-3

CMF C23 H22 Cl N5 O S

CDES 1:S

Absolute stereochemistry.



CM 2

CRN 64-17-5

CMF C2 H6 O

H₃C-CH₂-OH

IT **141269-30-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decompn. of)

RN 141269-30-9 CAPLUS

CN Butanedioic acid, 2,3-bis(benzoyloxy)-, [S-(R*,R*)]-, compd. with
(-)-6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-4H-
pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (1:1)
(9CI) (CA INDEX NAME)

CM 1

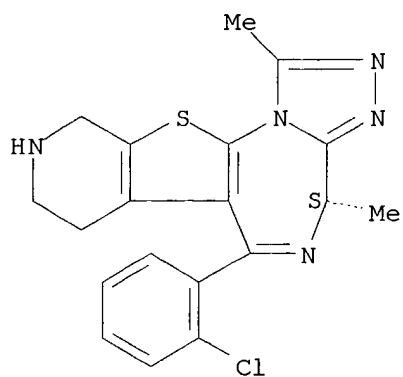
CRN 130311-76-1

CMF C19 H18 Cl N5 S

CDES 1:S

Absolute stereochemistry.

09/701,893

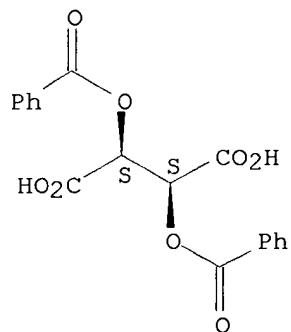


CM 2

CRN 17026-42-5

CMF C18 H14 O8

Absolute stereochemistry. Rotation (+).



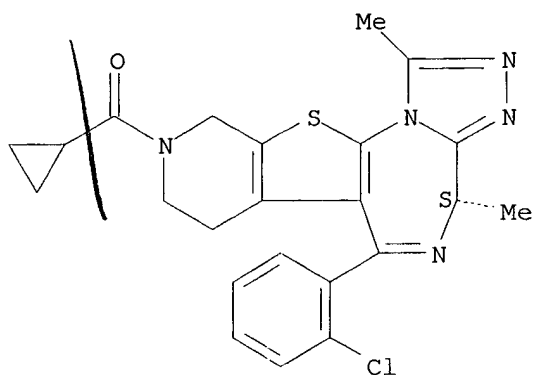
IT 131614-02-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., and mol. structure and abs. configuration of)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **130312-25-3**

RL: PROC (Process)

(resoln. of, using dibenzoyl-D-tartaric acid)

RN 130312-25-3 CAPLUS

IT **130311-77-2**

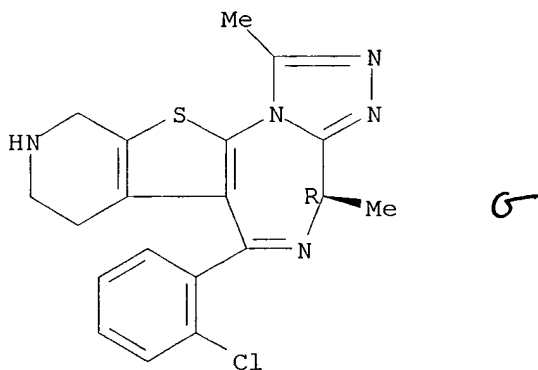
RL: PROC (Process)

(sepn. of, from enantiomer)

RN 130311-77-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



IT **130311-76-1**

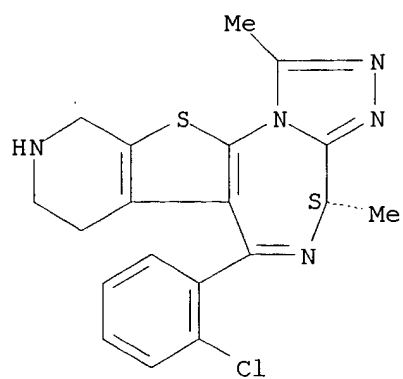
RL: PROC (Process)

(sepn. of, from enantiomer and N-acylation of, with cyclopropylcarbonyl
chloride)

RN 130311-76-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



9

L23 ANSWER 70 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:187545 CAPLUS

DN 116:187545

TI Demonstration of the participation of platelet-activating factor (PAF) in chloroquine retinopathy

AU Meyniel, Gaston; Doly, Michel; Millerin, Martine; Braquet, Pierre

CS Lab. Biophys., Fac. Med., Clermont-Ferrand, 63001, Fr.

SO C. R. Acad. Sci., Ser. III (1992), 314(2), 61-5

CODEN: CRASEV; ISSN: 0764-4469

DT Journal

LA French

AB Chloroquine retinopathy may result in loss of vision by alterations of the pigmentary epithelium and photoreceptors. The involvement of platelet-activating factor (PAF) in chloroquine-induced retinopathy and the use of PAF antagonists for prevention of this condition were studied using electroretinog. (ERG) of isolated rat retina. When retinas from normal rats were perfused with chloroquine (10-6M), a marked and rapid decrease in ERG b-wave amplitude was obsd. Chloroquine had no effect on the ERG of retina isolated from animals pretreated with the PAF antagonist BN 50730 (30 mg/kg/day i.p., 5 days). Chloroquine is a toxic drug for retinal function and PAF plays a key role in chloroquine retinopathy. PAF antagonists may constitute valuable agents for the treatment of this retinal impairment. The article has an abridged English version.

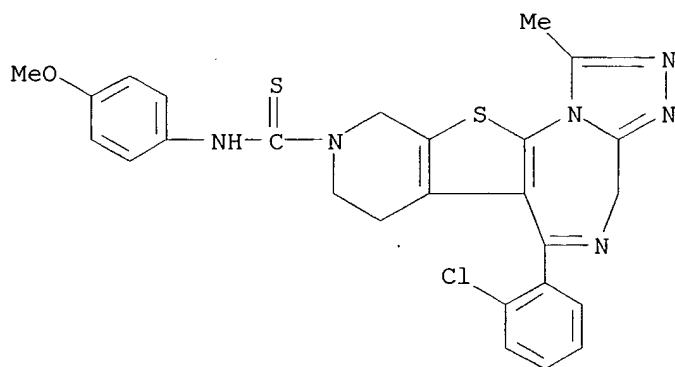
IT **132579-32-9**, BN-50730

RL: BIOL (Biological study)

(eye retinopathy from chloroquine prevention by)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 71 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:174118 CAPLUS

DN 116:174118

TI Structure-activity studies on triazolothienodiazepine derivatives as platelet-activating factor antagonists

AU Miyazawa, Shuhei; Okano, Kazuo; Shimomura, Naoyuki; Clark, Richard S. J.; Kawahara, Tetsuya; Asano, Osamu; Yoshimura, Hiroyuki; Miyamoto, Mituaki; Sakuma, Yoshinori; et al.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SO Chem. Pharm. Bull. (1991), 39(12), 3215-20

CODEN: CPBTAL; ISSN: 0009-2363

DT Journal

LA English

GI For diagram(s), see printed CA Issue.

AB Title compds. I (R = HC.tplbond.CCH₂, NCCMe₂O₂C, 4-FC₆H₄CH₂CO, etc., R₁ = R₂ = H; R = HC.tplbond.CCH₂CH₂O₂C, R₁, R₂ = H, Me, Et; R = NCCMe₂O₂C, cyclopropanecarbonyl, R₁ = Me, R₂ = H) were prepd. and their structure-activity relationship as platelet-activating factor antagonists was examd. Thus, I (R = R₁ = R₂ = H) reacted with HC.tplbond.CCH₂Br to give I (R = HC.tplbond.CCH₂). Introducing a Me group into the 8-position of the thienodiazepine nucleus leads to a longer duration of action.

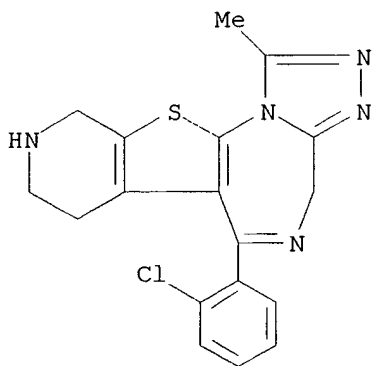
IT **114800-58-7**

RL: RCT (Reactant)

(alkylation and acylation of)

RN 114800-58-7 CAPLUS

CN 4H-Pyr:do[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



a

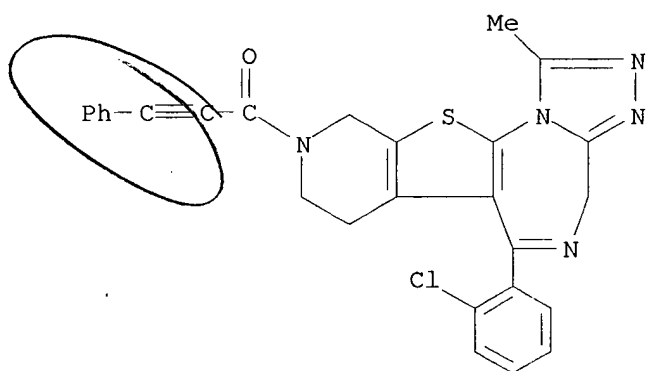
IT **130310-57-5 130310-63-3 140167-26-6****140167-27-7 140167-28-8**

RL: RCT (Reactant)

(platelet-activating factor antagonistic activity of)

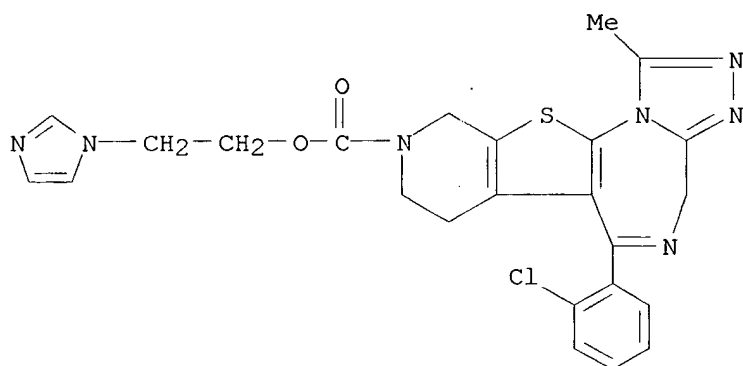
RN 130310-57-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(1-oxo-3-phenyl-2-propynyl)- (9CI) (CA INDEX NAME)



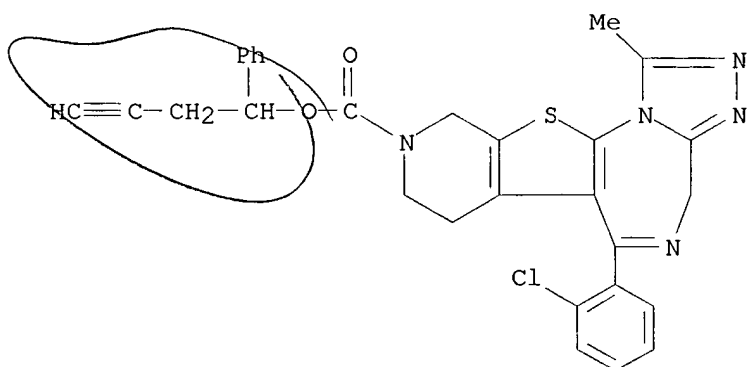
RN 130310-63-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-(1H-imidazol-1-yl)ethyl ester (9CI) (CA INDEX NAME)



RN 140167-26-6 CAPLUS

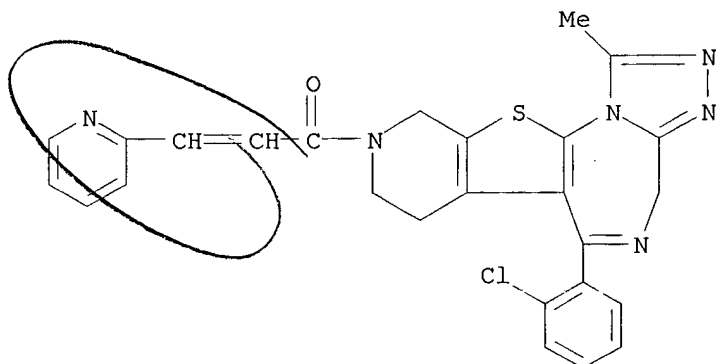
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 1-phenyl-3-butynyl ester (9CI) (CA INDEX NAME)



09/701,893

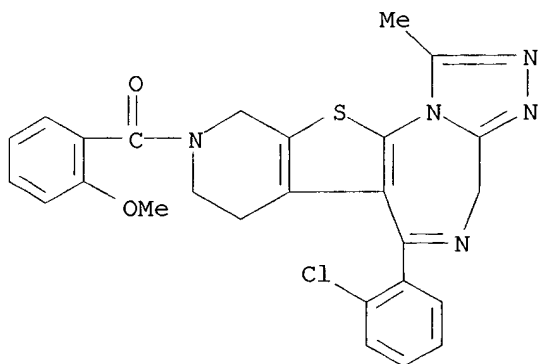
RN 140167-27-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-oxo-3-(2-pyridinyl)-2-
propenyl]- (9CI) (CA INDEX NAME)



RN 140167-28-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-(2-methoxybenzoyl)-1-methyl-
(9CI) (CA INDEX NAME)



b. 11111111

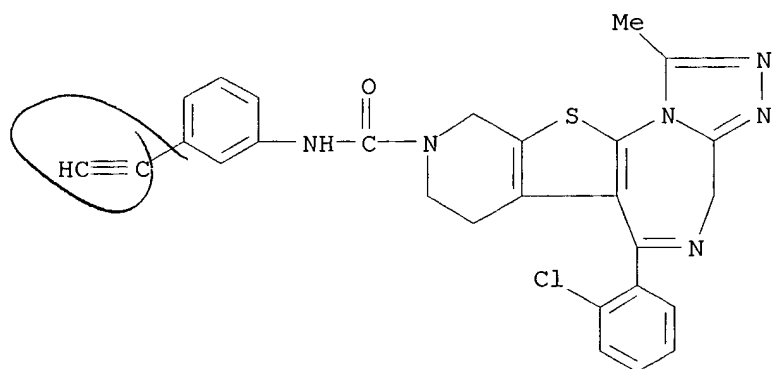
IT 130310-54-2 130335-42-1

RL: RCT (Reactant)

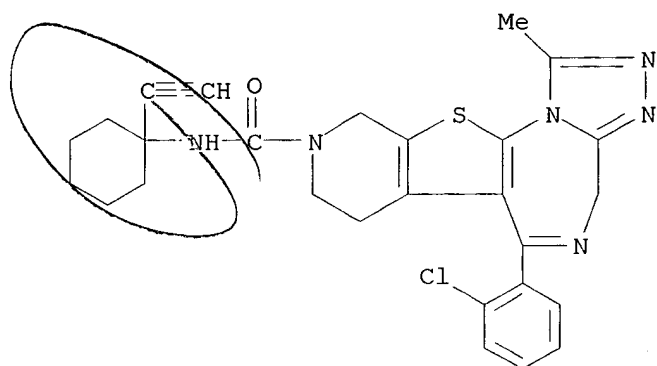
(platelet-activating, factor antagonistic activity of)

RN 130310-54-2 CAPLUS

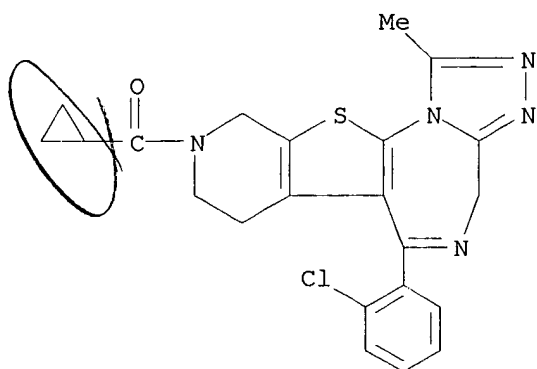
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(3-ethynylphenyl)-7,10-dihydro-1-
methyl- (9CI) (CA INDEX NAME)



RN 130335-42-1 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(1-ethynylcyclohexyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

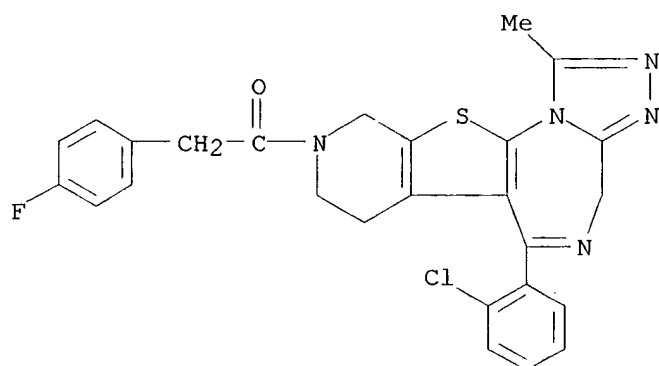


IT **130312-25-3P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and acylation of, with cyclopropionyl chloride)
 RN 130312-25-3 CAPLUS
 IT **130310-39-3P 130311-20-5P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and platelet-activating factor antagonistic activity of)
 RN 130310-39-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 130311-20-5 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-[(4-fluorophenyl)acetyl]-7,8,9,10-tetrahydro-1-methyl-
 (9CI) (CA INDEX NAME)

see 91 of 92

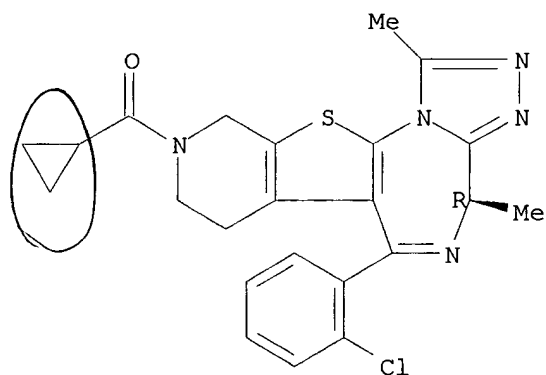


Proviso
 illll

IT 130311-02-3P 131614-02-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and platelet-activating factor inhibitory activity of)
 RN 130311-02-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
 dimethyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

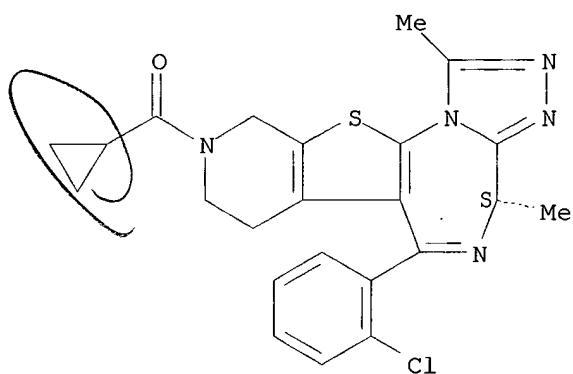
09/701,893



RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140224-77-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resoln. of)

RN 140224-77-7 CAPLUS

L23 ANSWER 72 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:128977 CAPLUS

DN 116:128977

TI Preparation of thienotriazolodiazepines as benzodiazepine receptor antagonists

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Pommier, Jacques

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Brit. UK Pat. Appl., 38 pp.

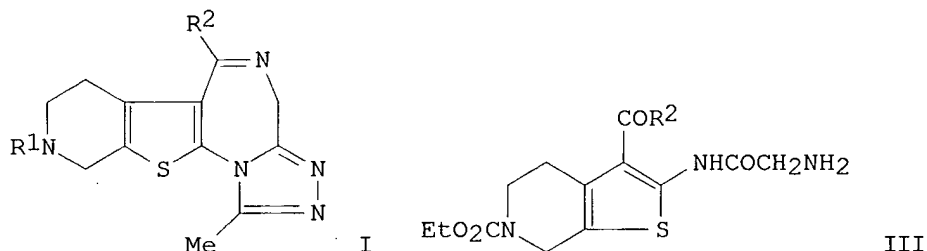
CODEN: BAXXDU

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2243829	A1	19911113	GB 1990-10402	19900509
	GB 2243829	B2	19930811		
	BE 1004123	A3	19920929	BE 1990-480	19900507
	CA 2016550	AA	19911111	CA 1990-2016550	19900511
	JP 04026691	A2	19920129	JP 1990-120189	19900511
PRAI	GB 1990-10402		19900509		
OS	MARPAT 116:128977				
GI					



AB Title compds. (I; R2 = 2-ClC6H4) [II; R1 = RSCH2C(:Y); R = alkyl, furyl, thienyl, (un)substituted Ph; Y = O, S] were prep'd. Thus, 2-ClC6H4COCH2CN (prepn. given) was cyclocondensed with N-ethoxycarbonyl-4-piperidone and S and the product converted into 2 steps to pyridothiophene III (R2 as above) which was cyclized and the product converted in 4 steps to II (R1 = Me2CHSCH2CO) II [R1 = 2-(F3C)C6H4SCH2CO] had IC50 of 6.36 .times. 10-9 (units not given) against PAF-induced platelet aggregation in vitro.

IT 128672-07-1 132522-27-1 132522-28-2
 132522-29-3 132522-30-6 132522-31-7
 132522-32-8 132522-33-9 132522-34-0
 132522-35-1 132522-36-2 132522-37-3
 132522-38-4 132522-39-5 132522-40-8
 132522-41-9 132522-42-0 132522-43-1
 132522-44-2 132522-45-3 132522-46-4
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 132522-50-0 132522-51-1 132522-52-2
 132522-53-3

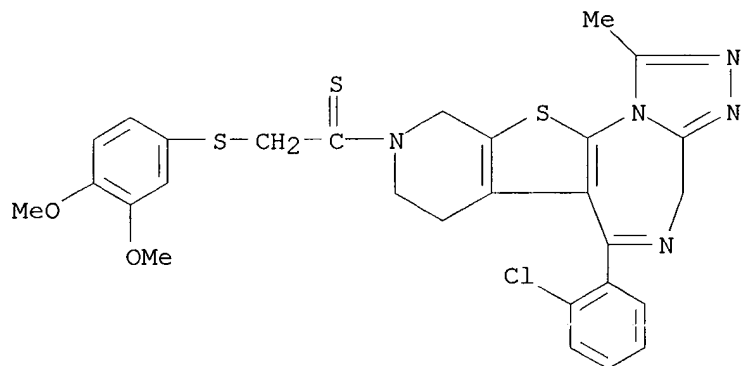
RL: RCT (Reactant)

(benzodiazepine receptor antagonist activity of)

RN 128672-07-1 CAPLUS

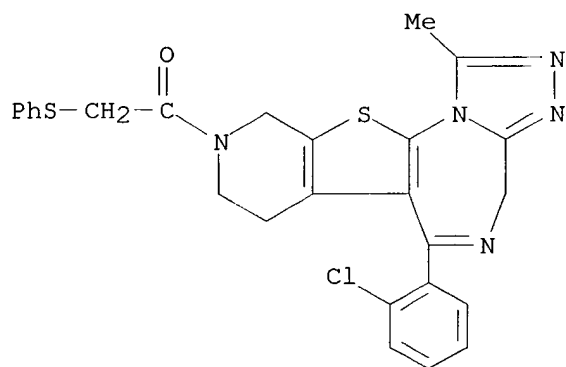
09/701,893

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-27-1 CAPLUS

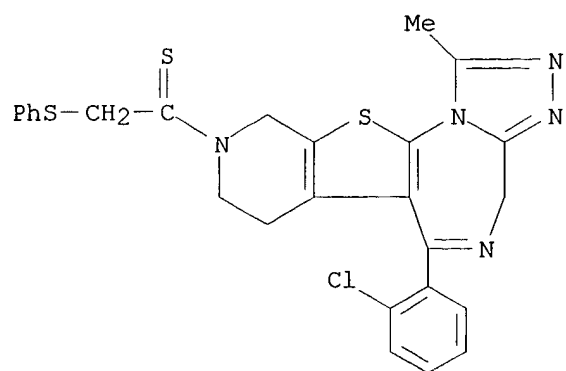
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(phenylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-28-2 CAPLUS

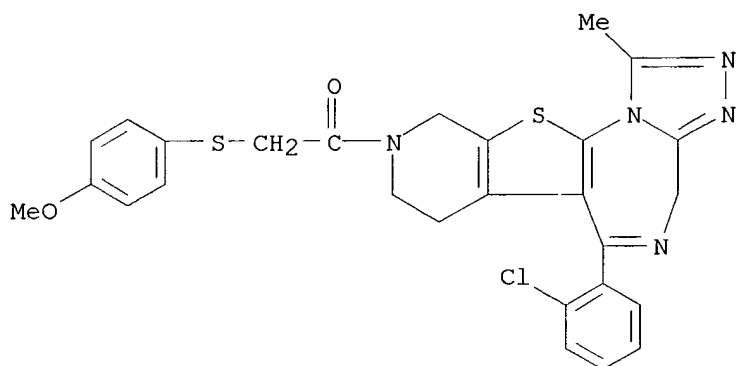
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(phenylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893



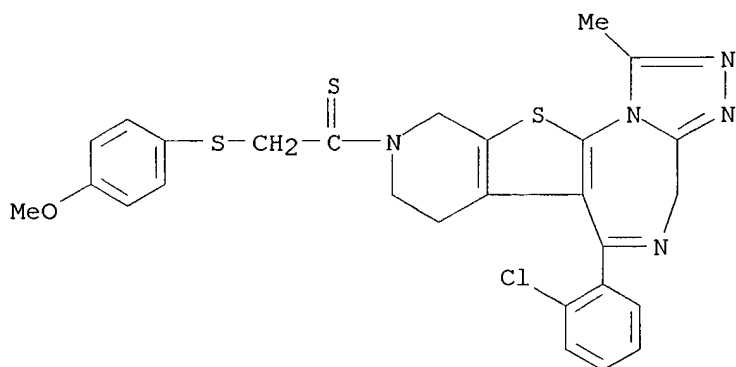
RN 132522-29-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(4-methoxyphenyl)thio]acetyl-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-30-6 CAPLUS

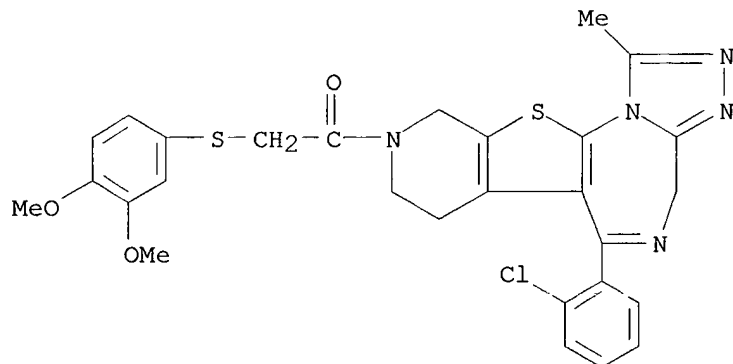
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[2-[(4-methoxyphenyl)thio]-1-
thioxoethyl]-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

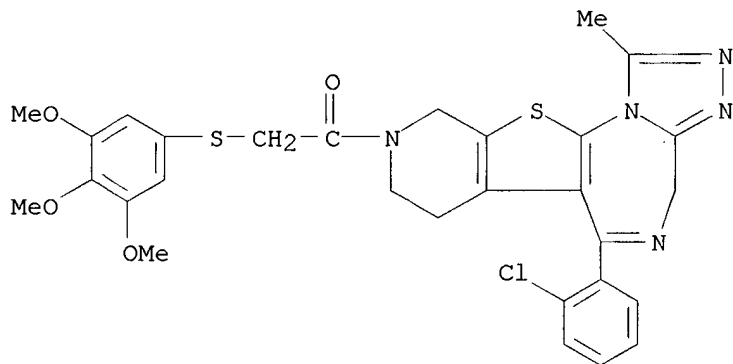
RN 132522-31-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[(3,4-dimethoxyphenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-32-8 CAPLUS

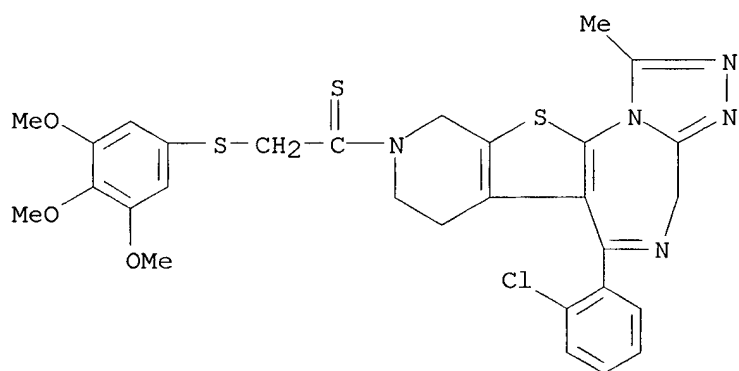
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(3,4,5-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-33-9 CAPLUS

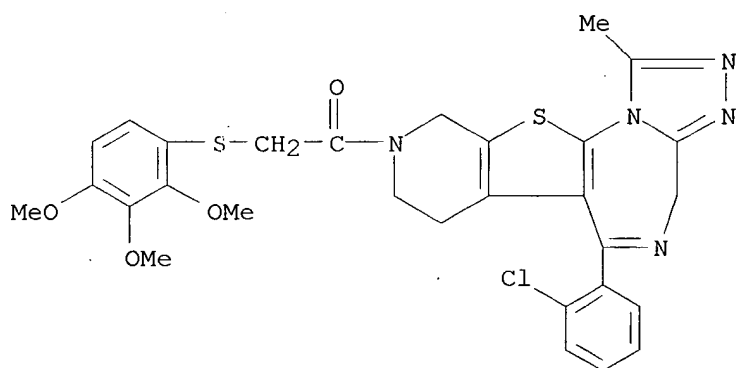
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(3,4,5-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)

09/701,893



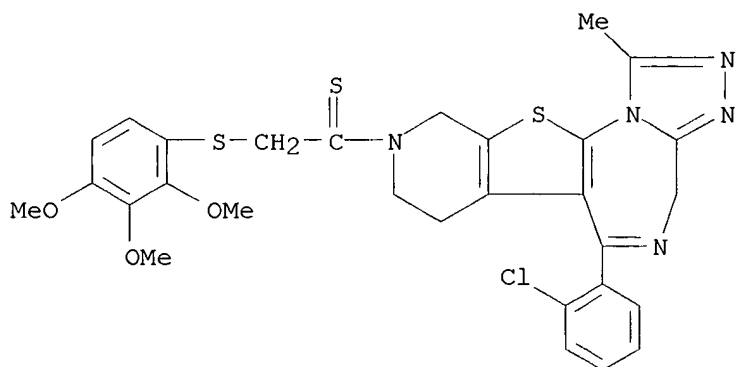
RN 132522-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2,3,4-
trimethoxyphenyl)thio]acetyl- (9CI) (CA INDEX NAME)



RN 132522-35-1 CAPLUS

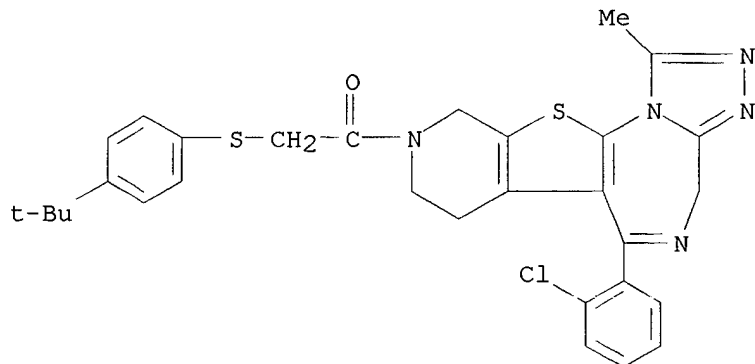
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(2,3,4-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



09/701,893

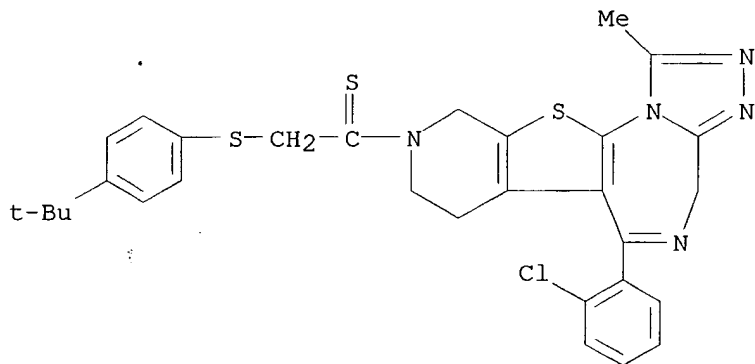
RN 132522-36-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(1,1-dimethylethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-37-3 CAPLUS

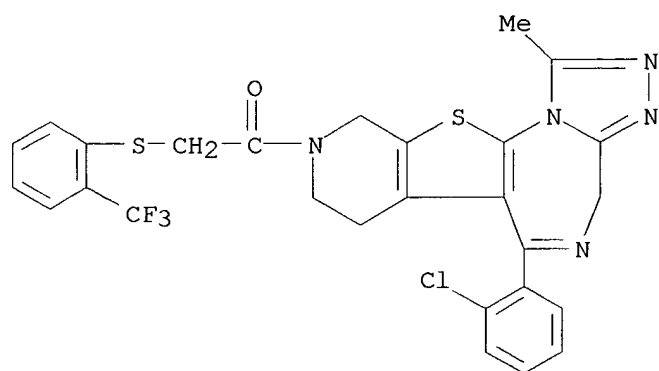
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[4-(1,1-dimethylethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-38-4 CAPLUS

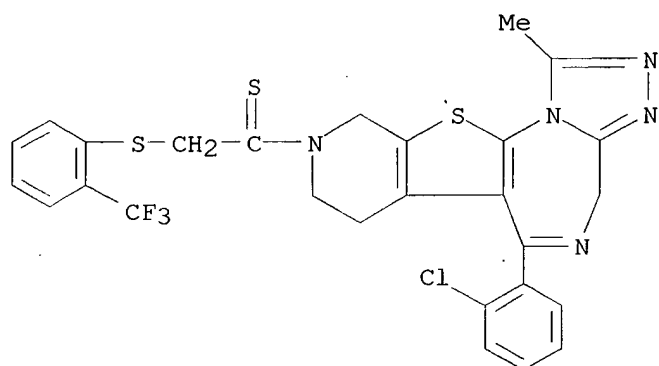
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[2-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)

09/701,893



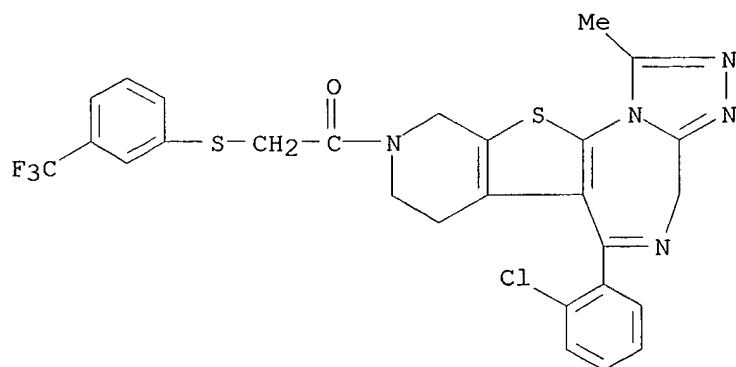
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CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[1-thioxo-2-[[2-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-40-8 CAPLUS

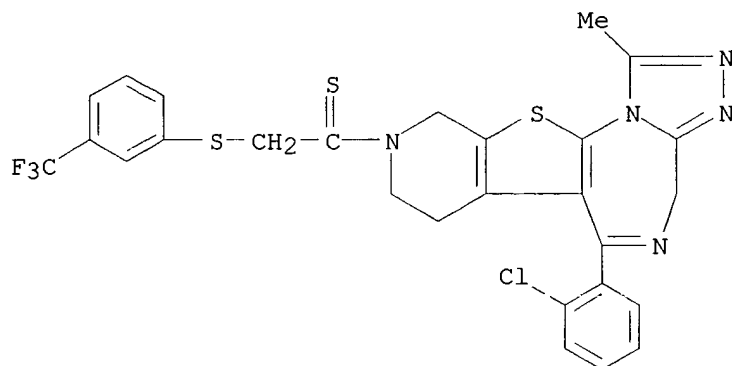
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[3-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



09/701,893

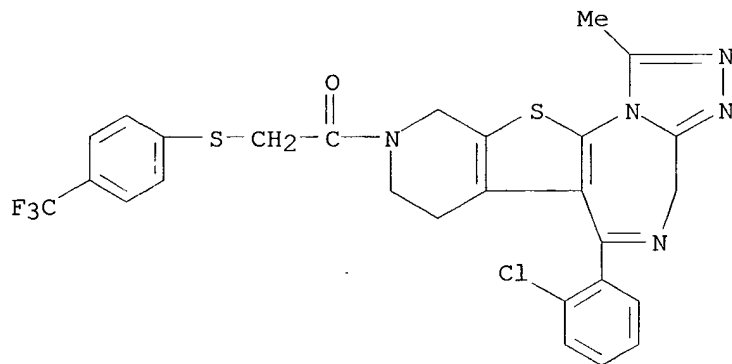
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CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[3-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



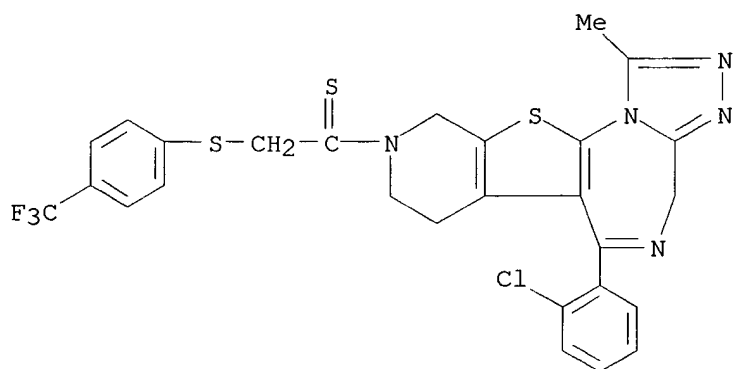
RN 132522-42-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[4-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



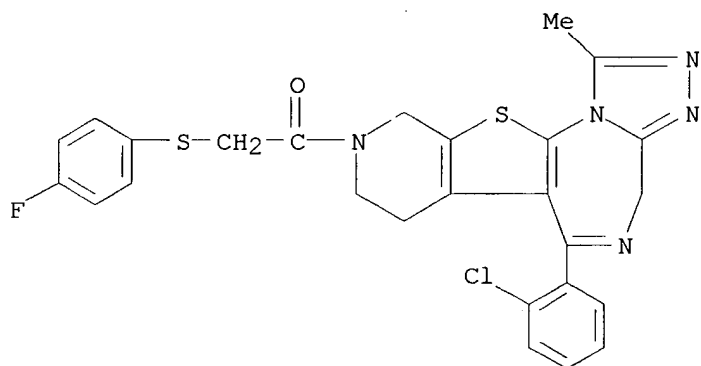
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CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[4-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



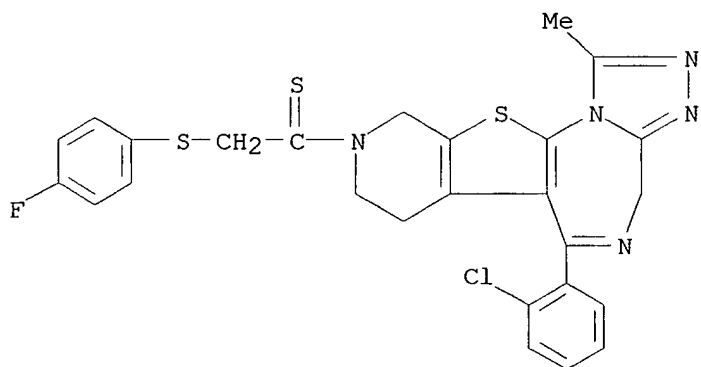
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6-(2-chlorophenyl)-9-[(4-fluorophenyl)thio]acetyl-7,8,9,10-tetrahydro-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-45-3 CAPLUS

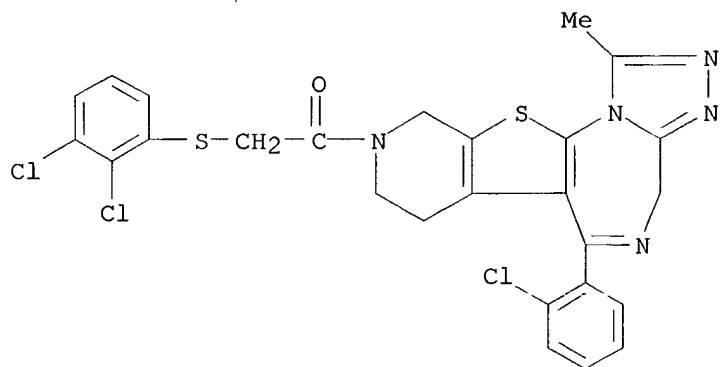
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6-(2-chlorophenyl)-9-[2-[(4-fluorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

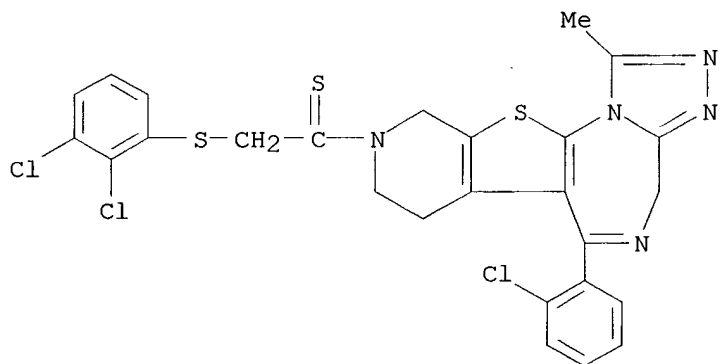
RN 132522-46-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[2-(2,3-dichlorophenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-47-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(2,3-dichlorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

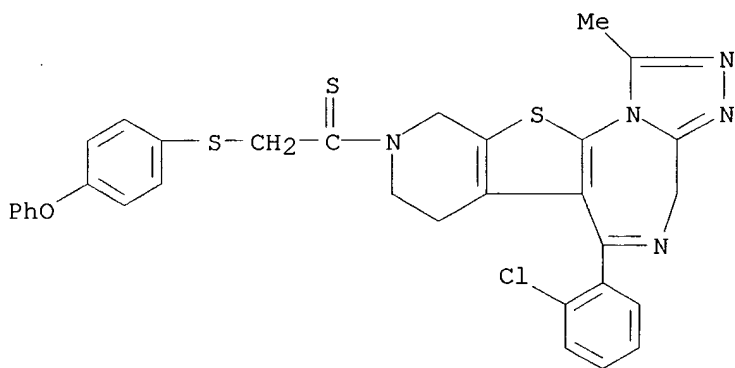


RN 132522-48-6 CAPLUS

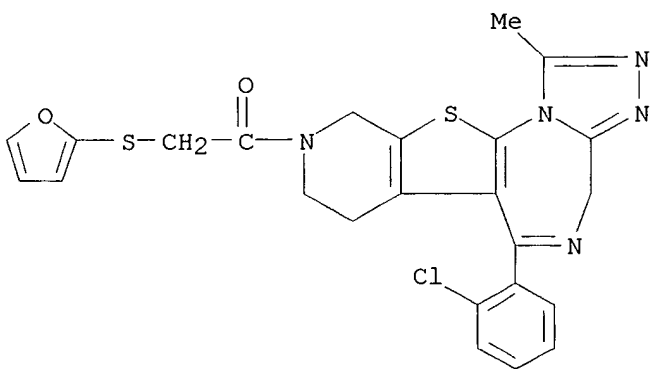
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phenoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)

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4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-[(4-
phenoxyphenyl)thio]-1-thioxoethyl]- (9CI) (CA INDEX NAME)



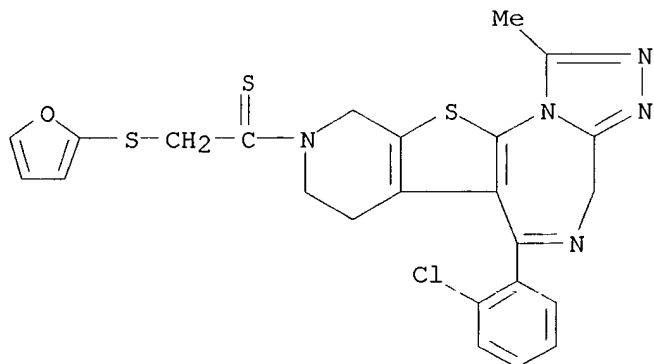
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09/701,893

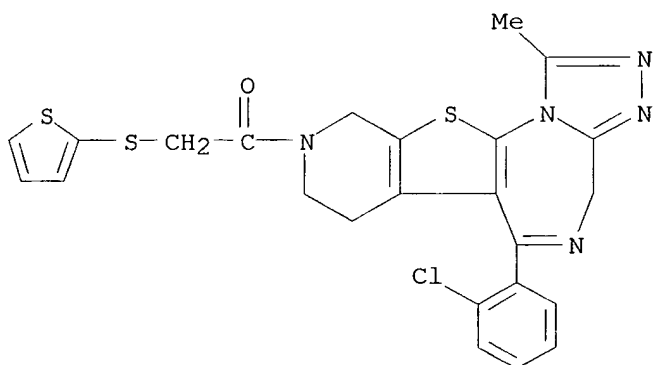
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RN 132522-52-2 CAPLUS

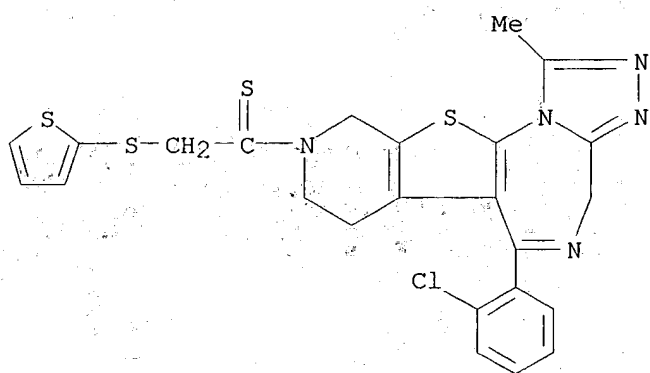
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RN 132522-53-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-thienylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893



L23 ANSWER 73 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:83705 CAPLUS

DN 116:83705

TI Preparation of 6-(2-chlorophenyl)-9-acyl-7,8,9,10-tetrahydro-1-methyl-4H-pyrido[4',3':4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]-1,4-diazepines

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Pommier, Jacques

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Ger. Offen., 17 pp.

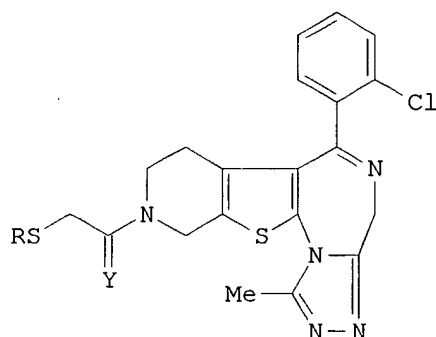
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DT Patent

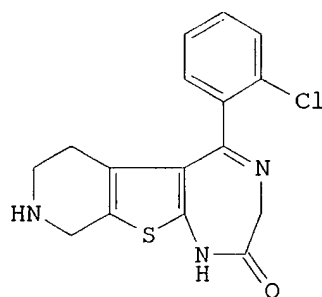
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4015136	A1	19911114	DE 1990-4015136	19900511
OS	MARPAT 116:83705				
GI					



I



II

AB Title compds. [I; Y = O, S; R = alkyl, (substituted) Ph, furyl, thienyl], were prepd. by (1) reaction of diazepinone II with 1 equiv RSCH₂CO₂H and excess DCC at 0-60.degree., (2) treatment of the acylated product with 3-5 equiv N₂H₄ in a protic solvent of room temp. -50.degree., (3) cyclocondensation of the resulting hydrazinimine with 1 or more equiv orthoacetate at room temp.-reflux, and (4) optional treatment of the product with 3-5 equiv P₂S₅. Thus, II (prepn. from NCCH₂CO₂H and 2-ClC₆H₄COCl given) in CH₂Cl₂ at 5.degree. was treated simultaneously with DCC in CH₂Cl₂ and with Me₂CHSCH₂CO₂H in CH₂Cl₂. The mixt. was stirred 30 min at ice temp. and then at 50.degree. to give 68% 8-acylated product, which was stirred 90 min with N₂H₄ in MeOH at room temp. 30 min at 40.degree., and 1 h at room temp. to give 83% hydrazinimine. This was refluxed with (EtO)₃CMe in MeOH to give 89% I (R = Me₂CH, Y = O). I inhibited PAF-induced blood platelet aggregation with IC₅₀ = (6.56 .times. 10⁻⁹)-(5.11 .times. 10⁻⁷) M.

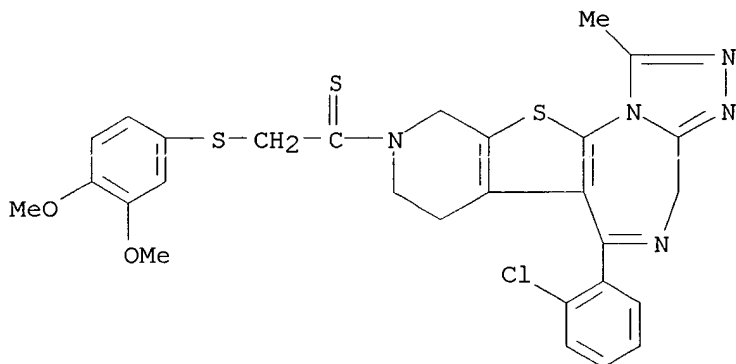
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 132522-50-0P 132522-51-1P 132522-52-2P

132522-53-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agent)

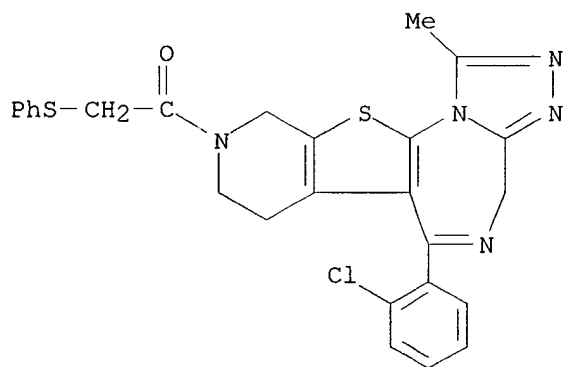
RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-27-1 CAPLUS

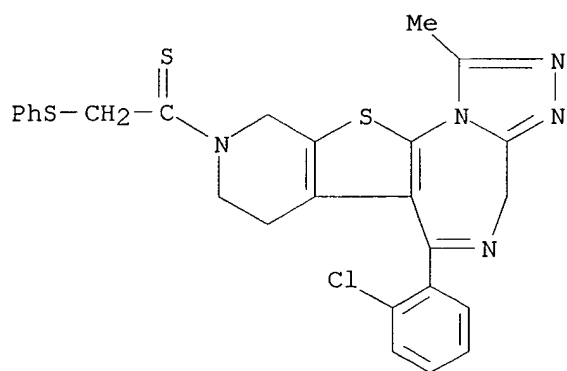
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(phenylthio)acetyl]- (9CI) (CA INDEX NAME)



RN 132522-28-2 CAPLUS

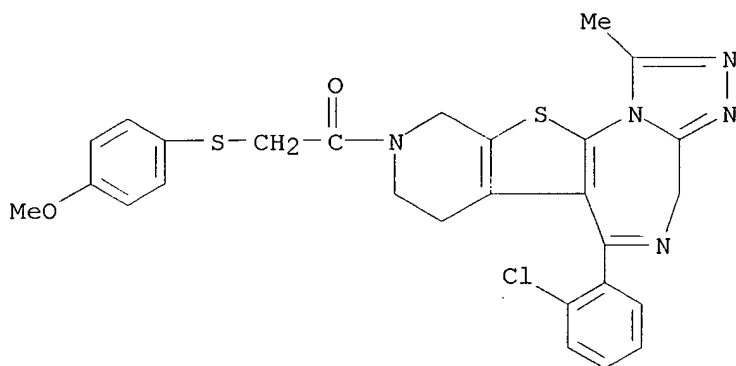
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(phenylthio)-1-thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893



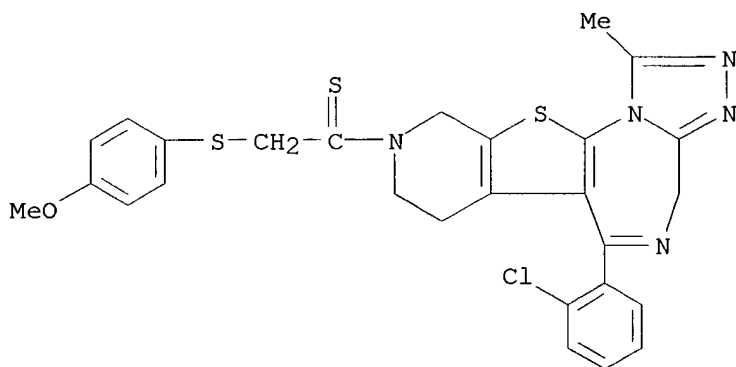
RN 132522-29-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[(4-methoxyphenyl)thio]acetyl-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-30-6 CAPLUS

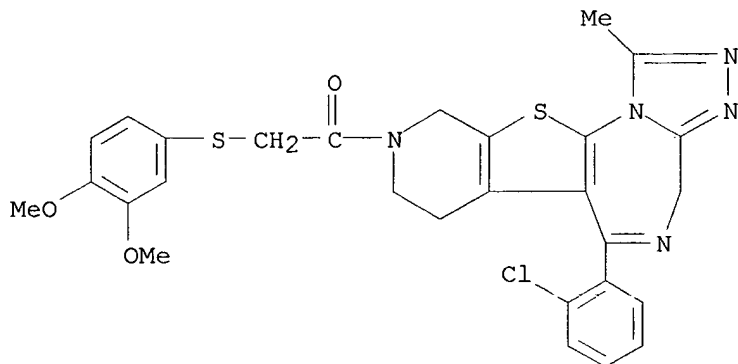
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[2-[(4-methoxyphenyl)thio]-1-
thioxoethyl]-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

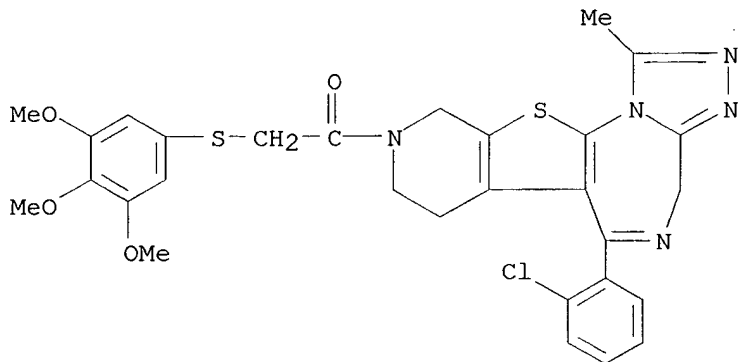
RN 132522-31-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[(3,4-dimethoxyphenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-32-8 CAPLUS

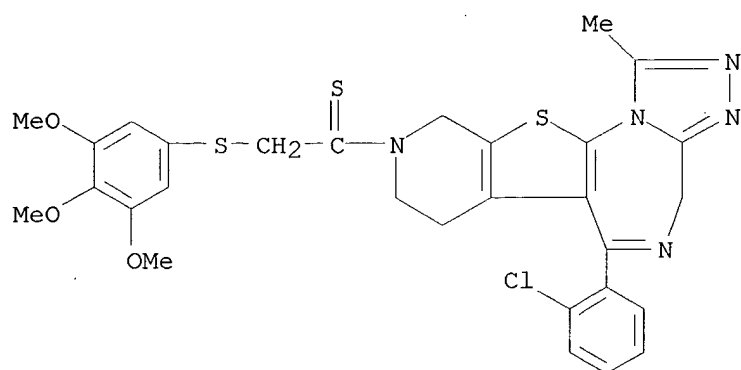
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(3,4,5-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-33-9 CAPLUS

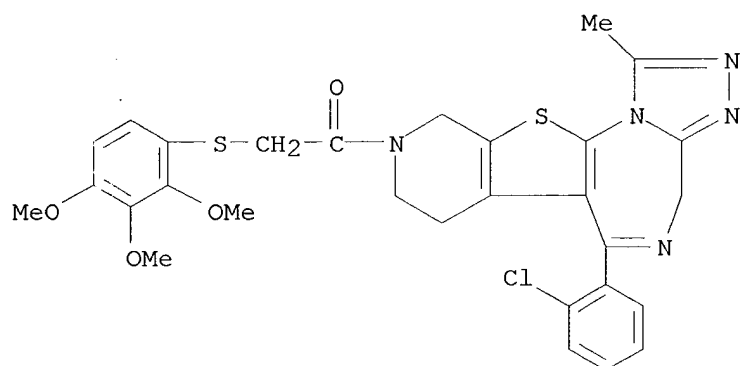
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(3,4,5-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)

09/701,893



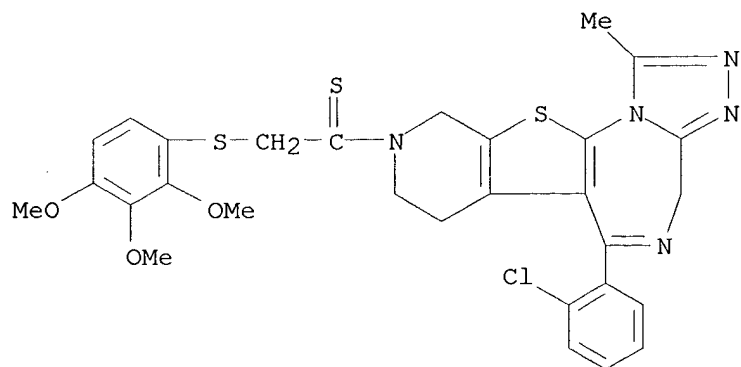
RN 132522-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2,3,4-
trimethoxyphenyl)thio]acetyl- (9CI) (CA INDEX NAME)



RN 132522-35-1 CAPLUS

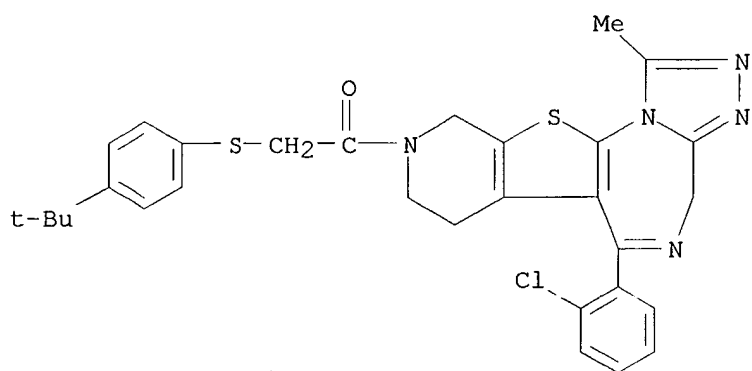
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(2,3,4-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



09/701,893

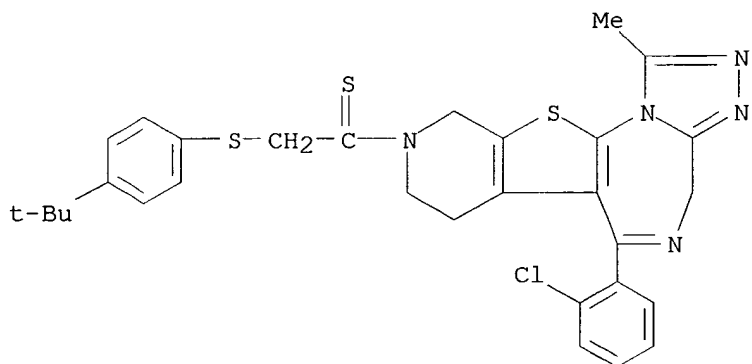
RN 132522-36-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(1,1-dimethylethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-37-3 CAPLUS

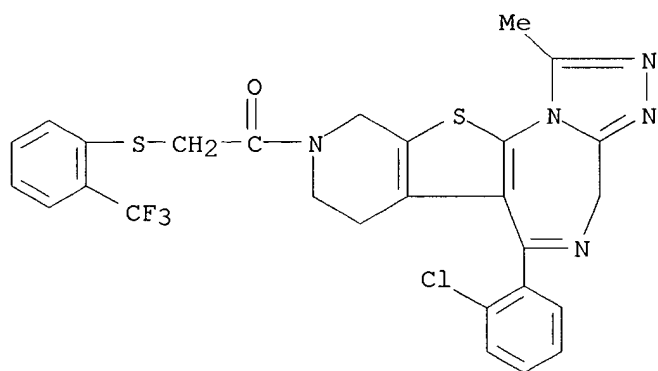
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[4-(1,1-dimethylethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-38-4 CAPLUS

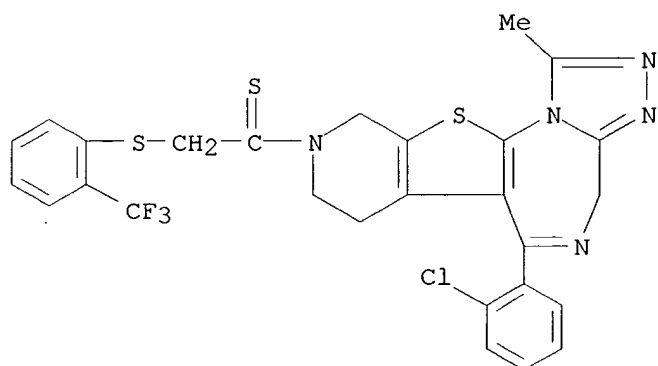
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[2-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)

09/701,893



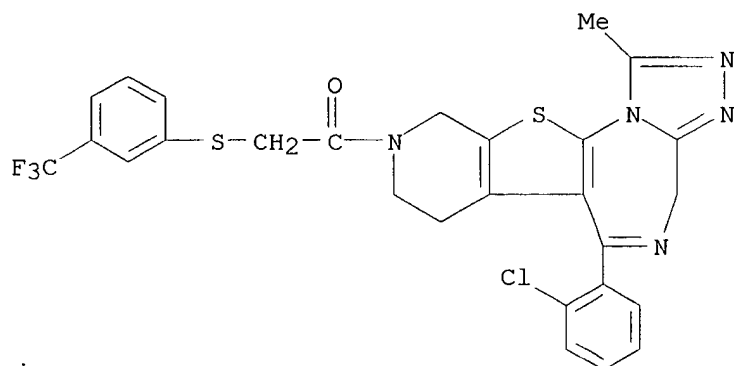
RN 132522-39-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[2-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-40-8 CAPLUS

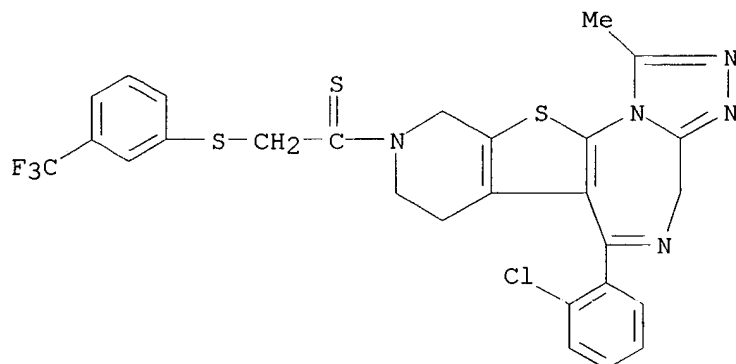
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[3-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



09/701,893

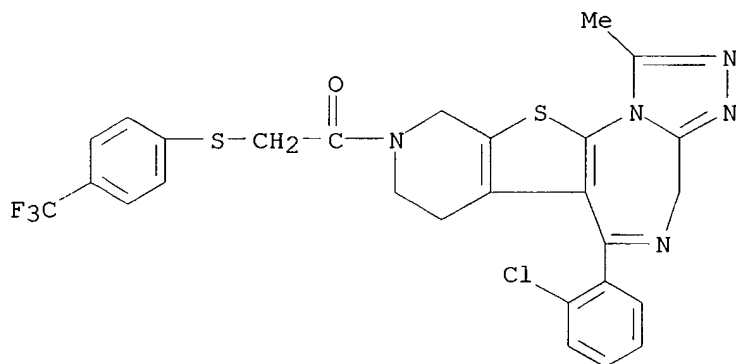
RN 132522-41-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[3-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-42-0 CAPLUS

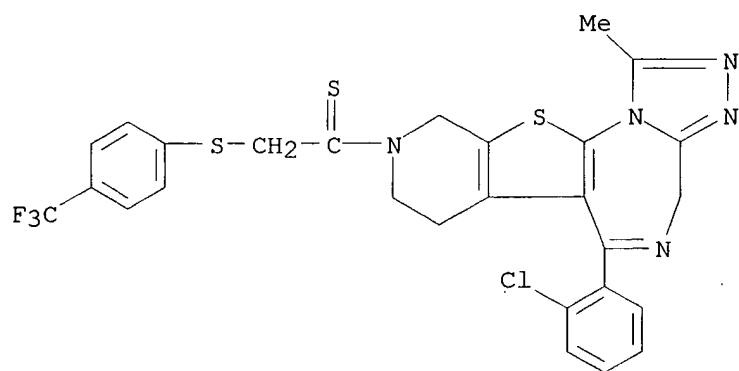
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[4-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-43-1 CAPLUS

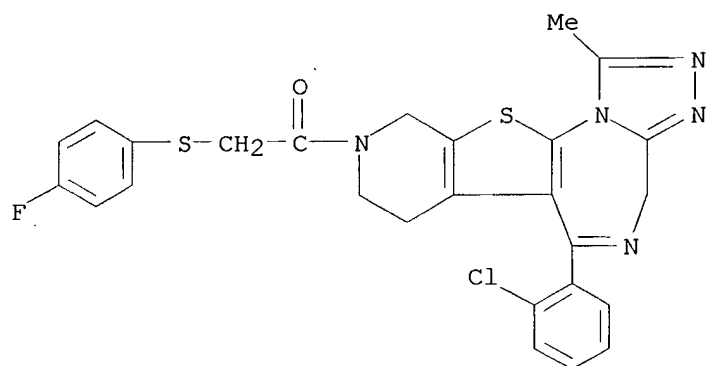
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[4-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)

09/701,893



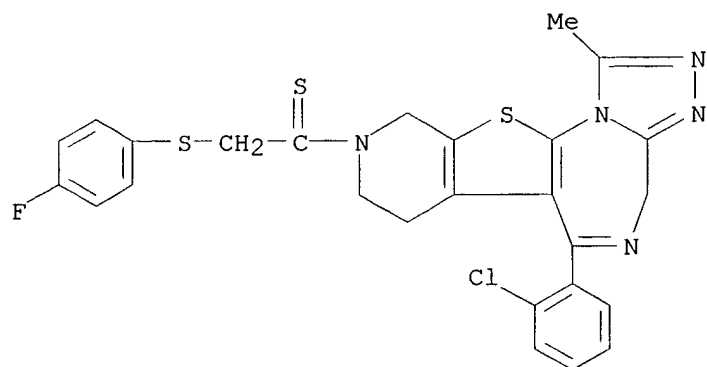
RN 132522-44-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(4-(trifluoromethyl)phenyl)thio]acetyl-7,8,9,10-tetrahydro-1-
methyl- (9CI) (CA INDEX NAME)



RN 132522-45-3 CAPLUS

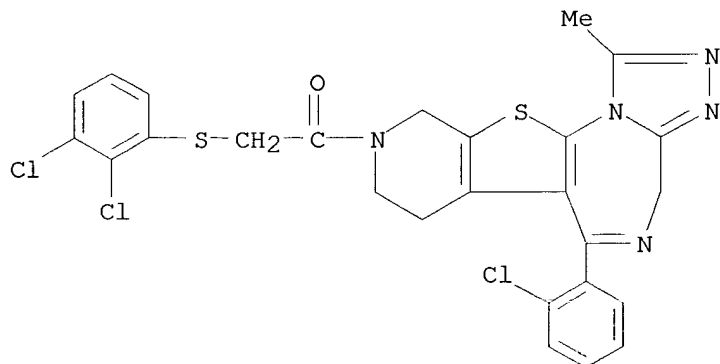
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(4-fluorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

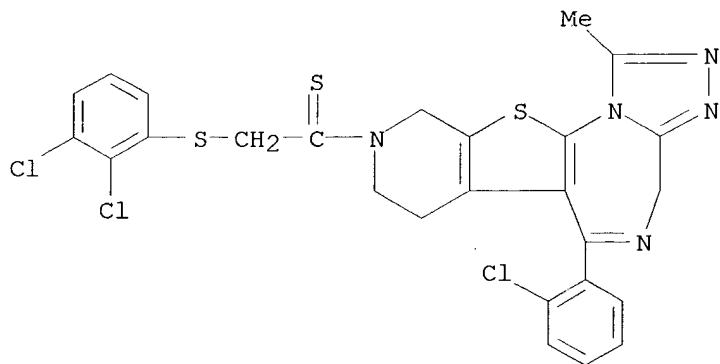
RN 132522-46-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[(2,3-dichlorophenyl)thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-47-5 CAPLUS

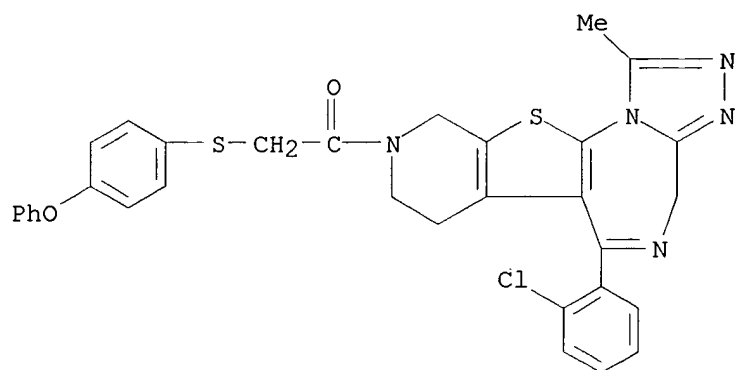
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(2,3-dichlorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-48-6 CAPLUS

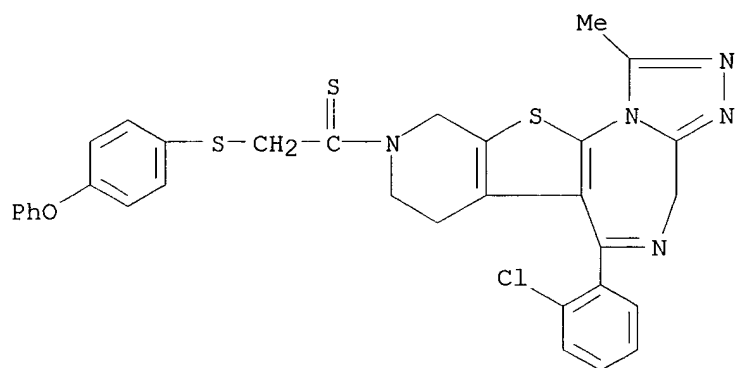
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(4-
phenoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)

09/701,893



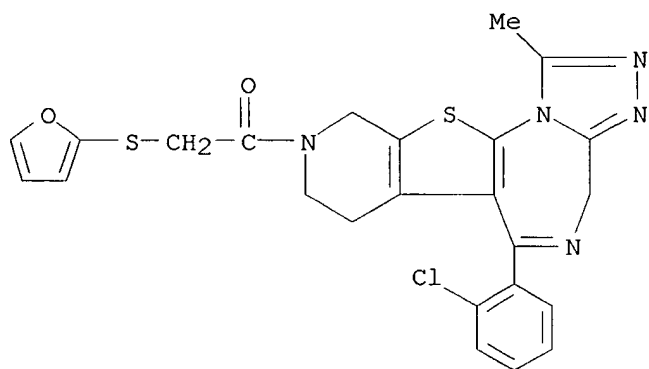
RN 132522-49-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(4-
phenoxyphenyl)thio]-1-thioxoethyl]- (9CI) (CA INDEX NAME)



RN 132522-50-0 CAPLUS

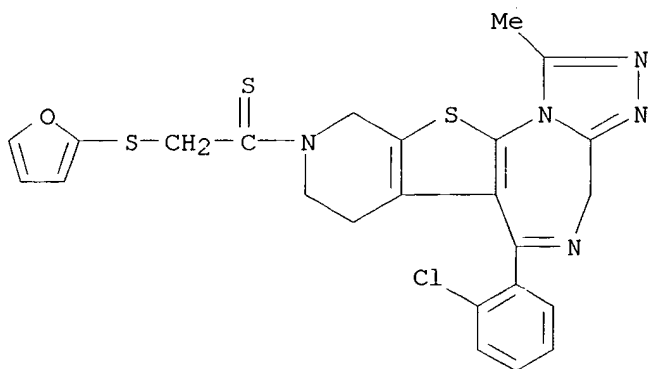
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(2-furanylthio)acetyl]-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



09/701,893

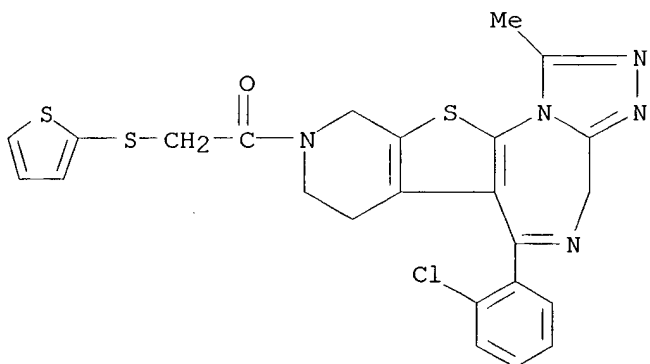
RN 132522-51-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-(2-furanylthio)-1-thioxoethyl]-7,8,9,10-tetrahydro-
1-methyl- (9CI) (CA INDEX NAME)



RN 132522-52-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-thienylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-53-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-thienylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)

09/701,893

~~DI~~3 ANSWER 74 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1992:51275 CAPLUS

DN 116:51275

TI Inhibitory effects of a novel PAF antagonist E6123 on anaphylactic responses in passively and actively sensitized guinea pigs and passively sensitized mice

AU Sakuma, Y.; Muramoto, K.; Harada, K.; Katayama, S.; Tsunoda, H.; Katayama, K.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300, Japan

SO Prostaglandins (1991), 42(6), 541-55

CODEN: PRGLBA; ISSN: 0090-6980

DT Journal

LA English

AB The effects of the platelet-activating factor (PAF) antagonist, E6123, on anaphylactic responses in guinea pigs and mice were investigated. E6123 inhibited i.v. antigen (Ag)- or inhaled Ag-induced bronchoconstriction in passively and actively sensitized guinea pigs after oral administration at 3 and 10 .mu.g/kg, resp. E6123 inhibited Ag inhalation-induced airway hyperreactivity in guinea pigs after oral administration at 30 .mu.g/kg. E6123 protected mice from anaphylactic death with an ED50 value (oral) of 7 .mu.g/kg. The inhibitory effects of E6123 described above were very potent compared to those of the PAF-antagonists WEB2347 and Y-24180. The present results suggest that E6123 may be beneficial for the treatment of asthma, a condition in which PAF is assumed to be involved.

IT **131614-02-3**, E6123

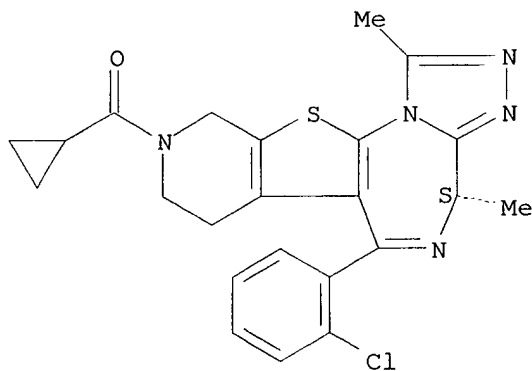
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(anaphylactic and antiasthmatic activity of)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 75 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1992:41492 CAPLUS

DN 116:41492

TI Preparation of 6-(2-chlorophenyl)-9-carbamoyl-7,8,9,10-tetrahydro-1-methyl-4H-pyrido[4',3',4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]-1,4-diazepines as PAF antagonists

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Rolland, Alain

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Brit. UK Pat. Appl., 31 pp.

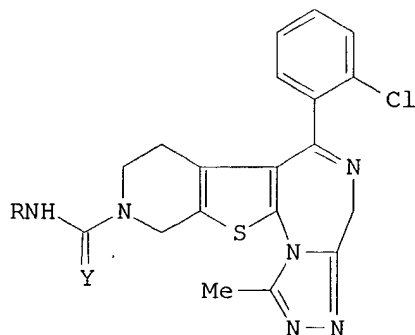
CODEN: BAXXDU

DT Patent

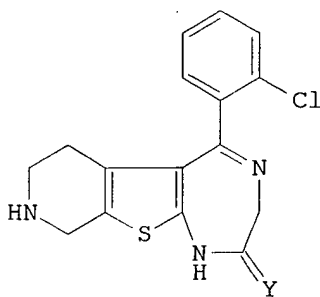
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2242427	A1	19911002	GB 1990-7001	19900329
	GB 2242427	B2	19930512		
OS	MARPAT 116:41492				
GI					



I



II

AB Title compds. [I; R = (cyclo)alkyl, alkenyl, (hetero)arylalkyl, (substituted) Ph, heterobicycyl, PhSO₂, heteroarylsulfonyl, bicycylsulfonyl; Y = O, S] were prepd. from (thio)lactams II by successive condensation with excess RNCY, N₂H₄, and (EtO)₃CMe. Thus, II (Y = S) [prepn. starting from NCCH₂CO₂H and 2-ClC₆H₄COCl via 2-(NCCH₂CO)C₆H₄Cl and 2-amino-3-(2-chlorobenzoyl)-6-ethoxycarbonyl-4,5,6,7-tetrahydropyrido[3,4-b]thiophene given] in MeOH was refluxed with 4-MeOC₆H₄NCS to give 83% acylated product. The latter was treated with N₂H₄ in THF to give 86% hydrazone, which was refluxed with (EtO)₃CMe in EtOH to give 92% I (R = 4-MeOC₆H₄). I orally inhibited platelet activating factor-induced bronchoconstriction in guinea pigs by 38.5-83.5%.

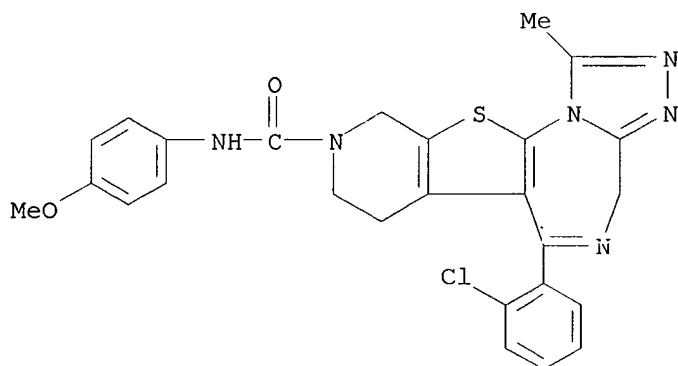
IT 132418-35-0P 132418-36-1P 132418-37-2P
 132418-38-3P 132418-39-4P 132418-40-7P
 132418-41-8P 132418-42-9P 132418-43-0P
 132418-44-1P 132418-45-2P 132418-46-3P
 132418-47-4P 132418-48-5P 132418-49-6P
 132418-50-9P 132418-51-0P 132418-52-1P
 132418-53-2P 132418-54-3P 132418-55-4P
 132418-56-5P 132418-58-7P 132418-59-8P
 132418-60-1P 132418-61-2P 132418-62-3P
 132418-64-5P 132442-67-2P 138192-67-3P

09/701,893

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as PAF antagonist, from pyridothienodiazepinone precursor)

RN 132418-35-0 CAPLUS

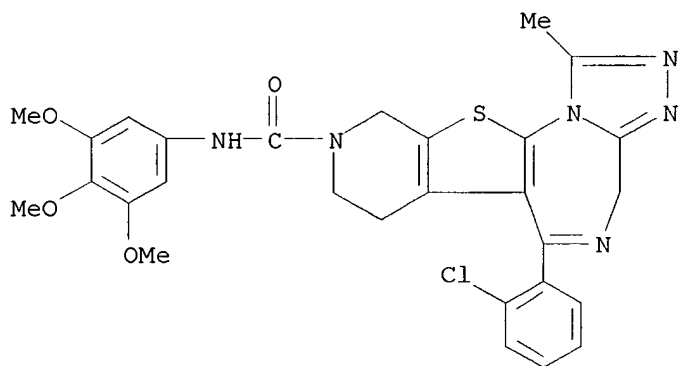
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-36-1 CAPLUS

RN 132418-37-2 CAPLUS

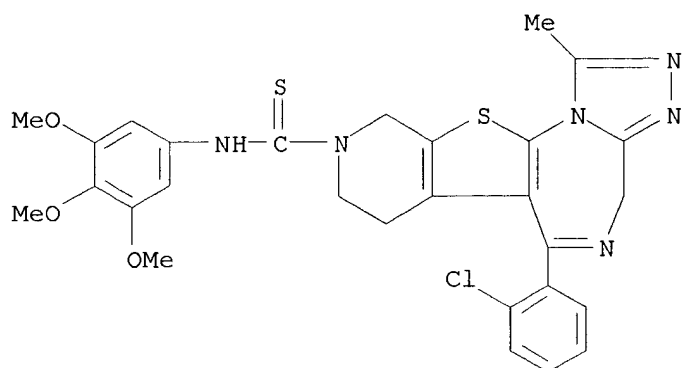
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 132418-38-3 CAPLUS

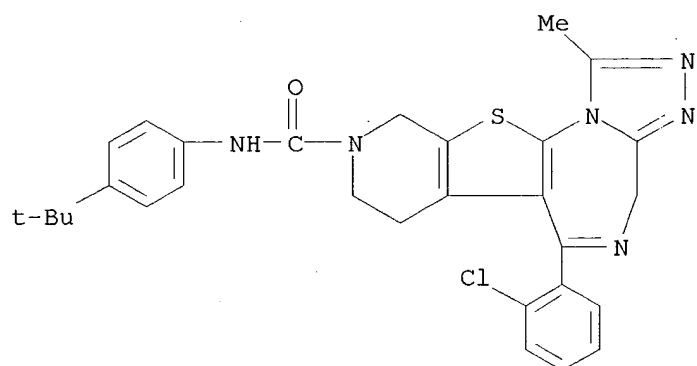
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

09/701,893



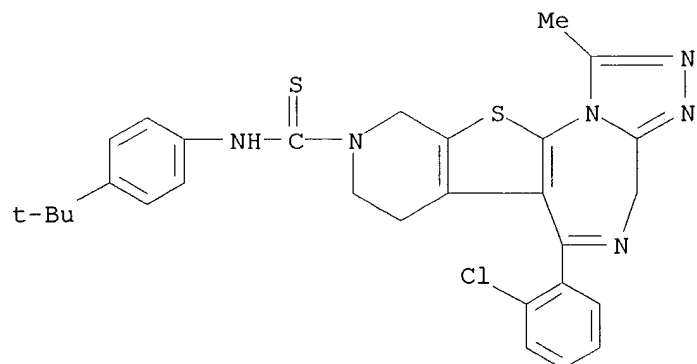
RN 132418-39-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-40-7 CAPLUS

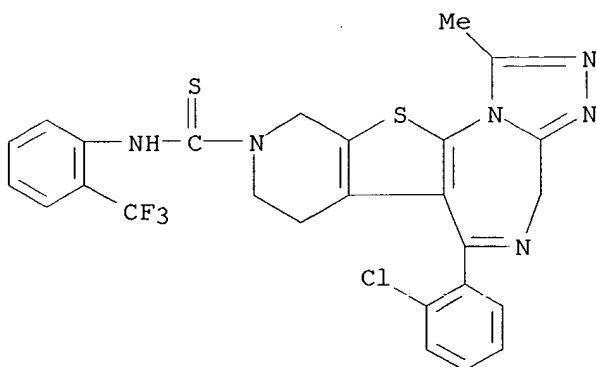
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-(1,1-dimethylethyl)phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

RN 132418-41-8 CAPLUS

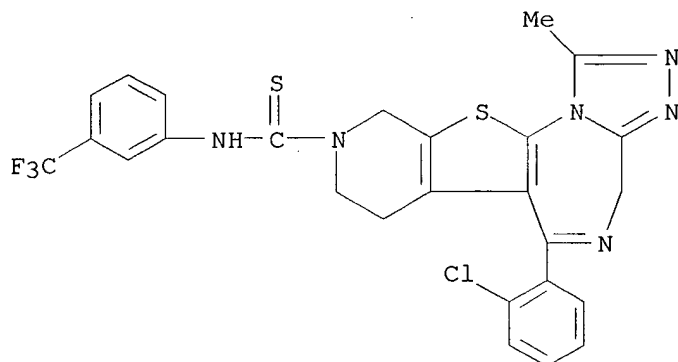
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



bii

RN 132418-42-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

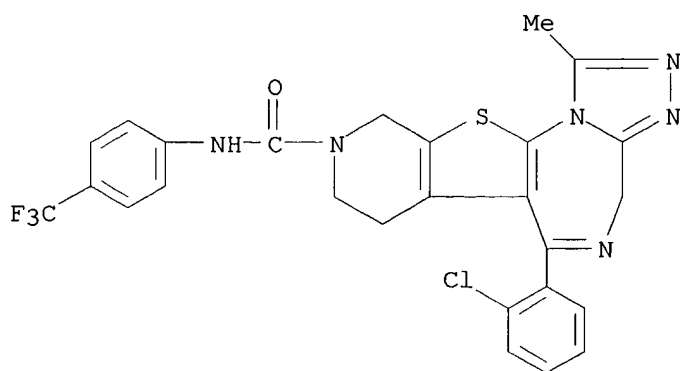


bii

RN 132418-43-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

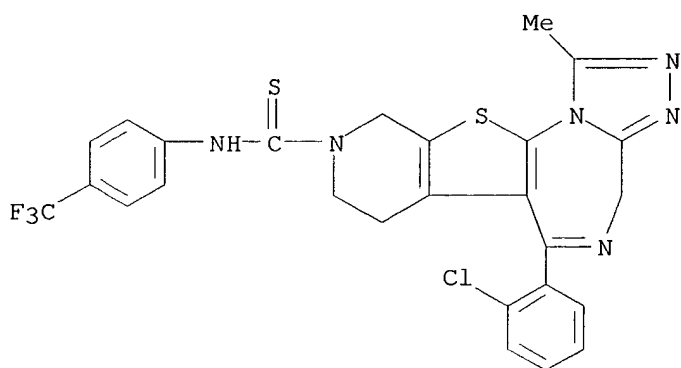
09/701,893



b₂

RN 132418-44-1 CAPLUS

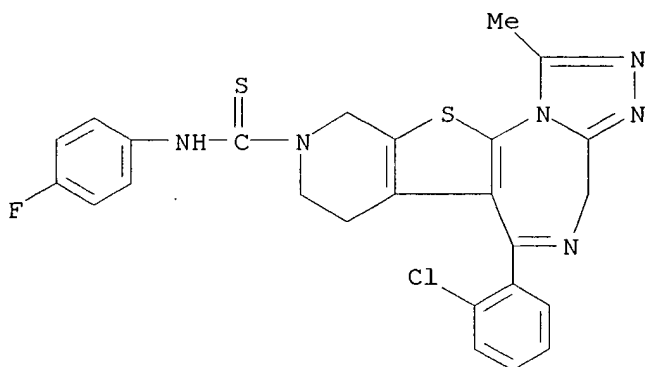
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



b₂

RN 132418-45-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-fluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

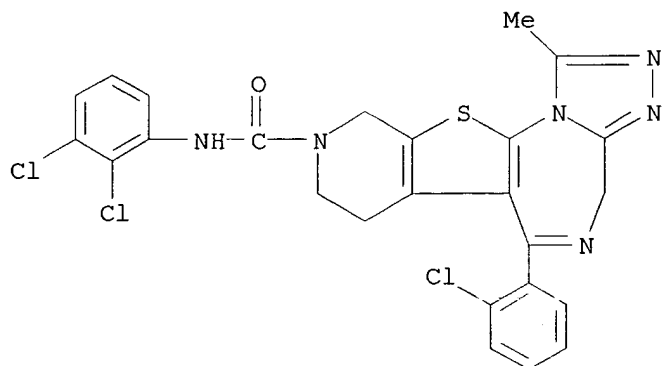


b₂

09/701,893

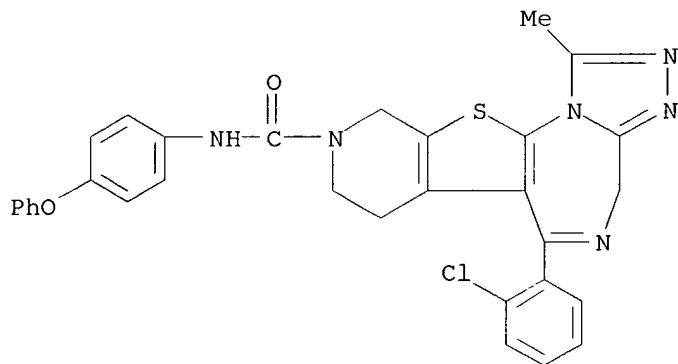
RN 132418-46-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,3-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-47-4 CAPLUS

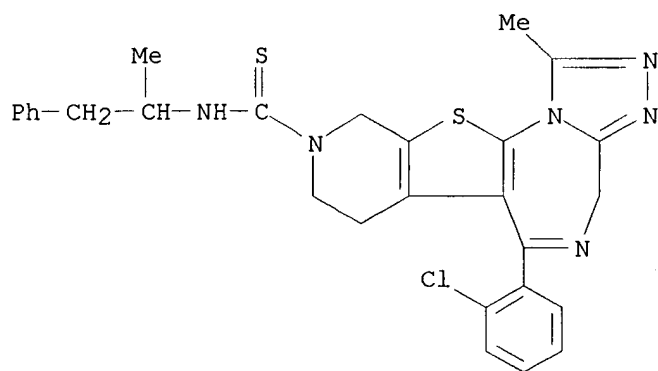
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 132418-48-5 CAPLUS

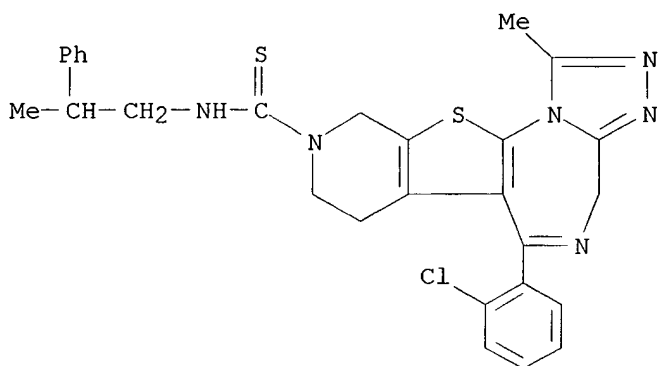
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1-methyl-2-phenylethyl)- (9CI) (CA INDEX NAME)

09/701,893



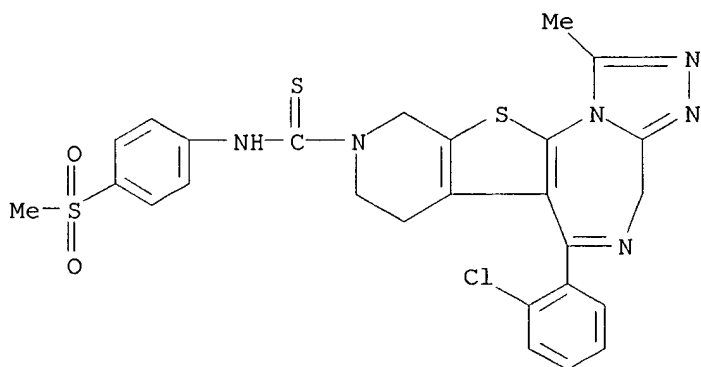
RN 132418-49-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-phenylpropyl)- (9CI) (CA INDEX NAME)



RN 132418-50-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

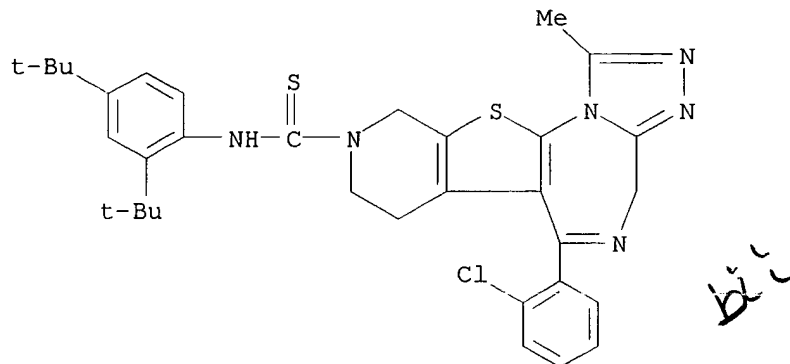


bcc

09/701,893

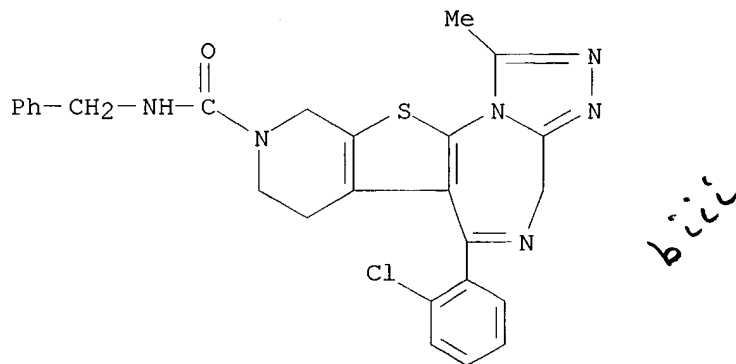
RN 132418-51-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[2,4-bis(1,1-dimethylethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



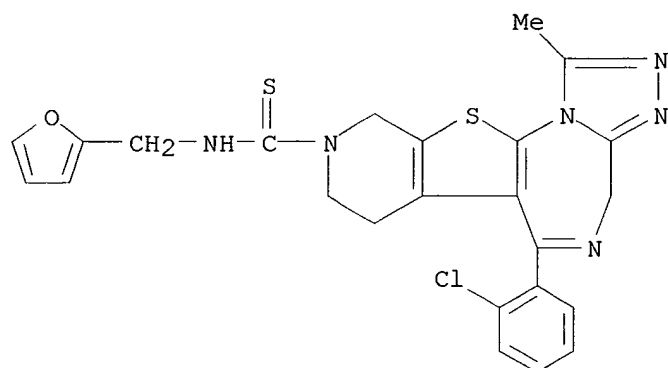
RN 132418-52-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



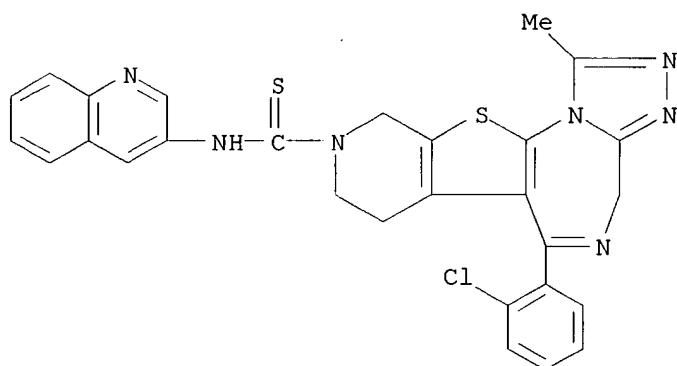
RN 132418-53-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylmethyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



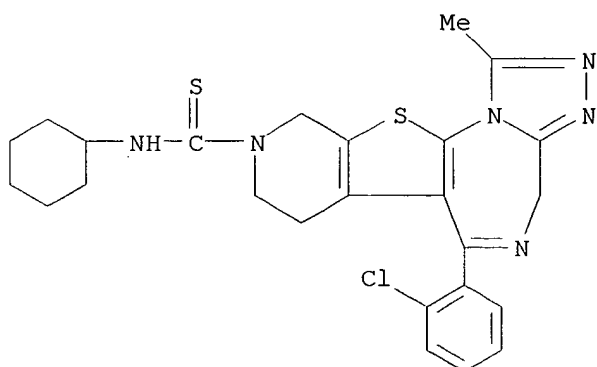
RN 132418-54-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-3-quinoliny- (9CI) (CA INDEX NAME)



RN 132418-55-4 CAPLUS

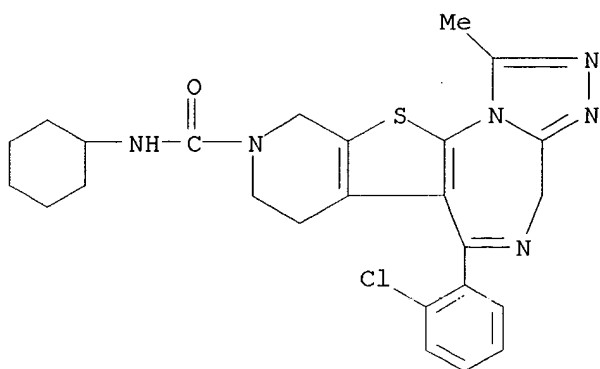
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

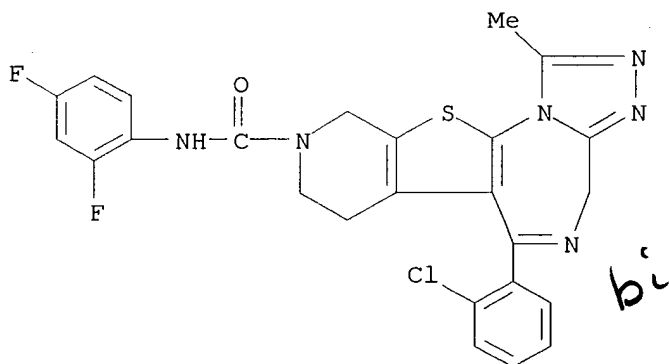
RN 132418-56-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl-(9CI) (CA INDEX NAME)



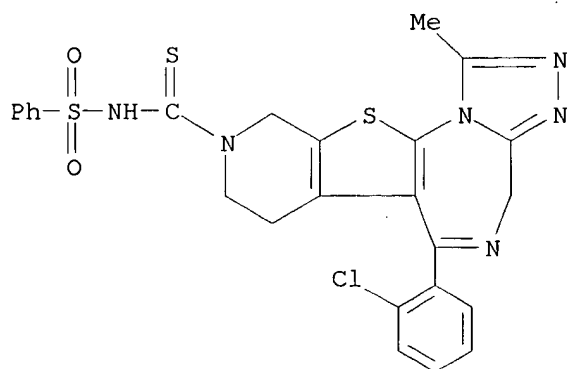
RN 132418-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,4-difluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



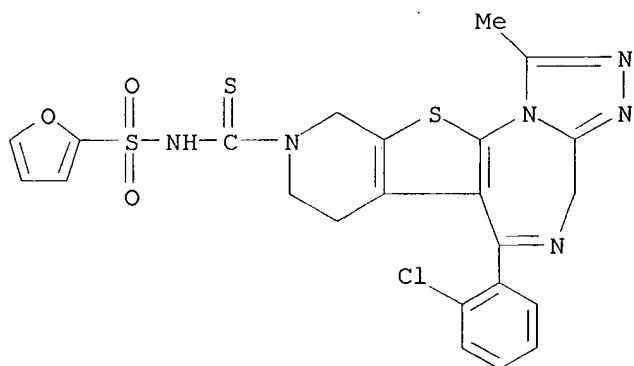
RN 132418-59-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



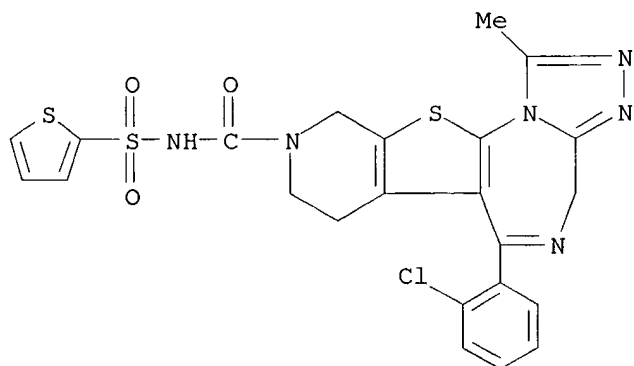
RN 132418-60-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylsulfonyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-61-2 CAPLUS

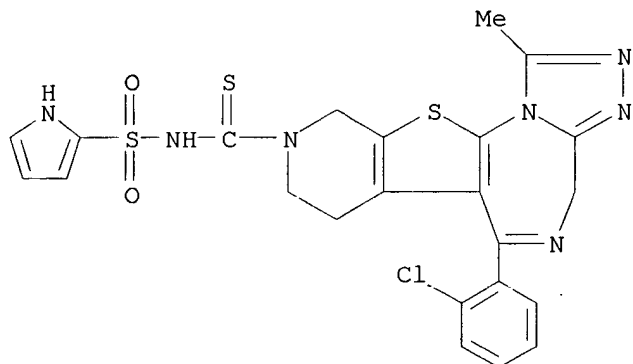
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



09/701,893

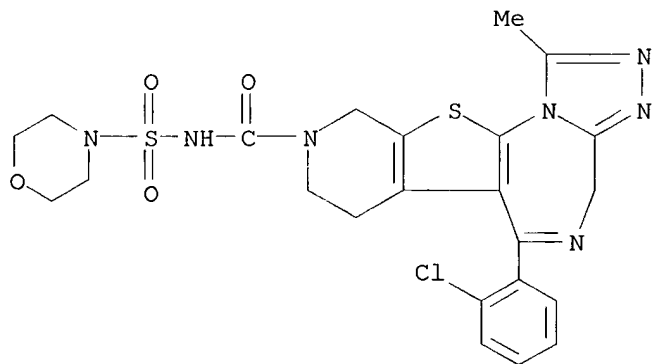
RN 132418-62-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1H-pyrrol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)



RN 132418-64-5 CAPLUS

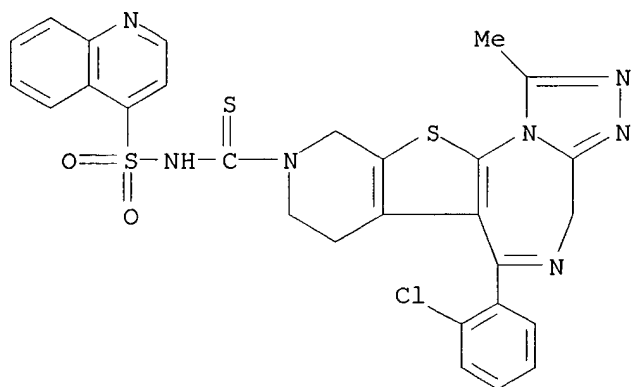
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-morpholinylsulfonyl)- (9CI) (CA INDEX NAME)



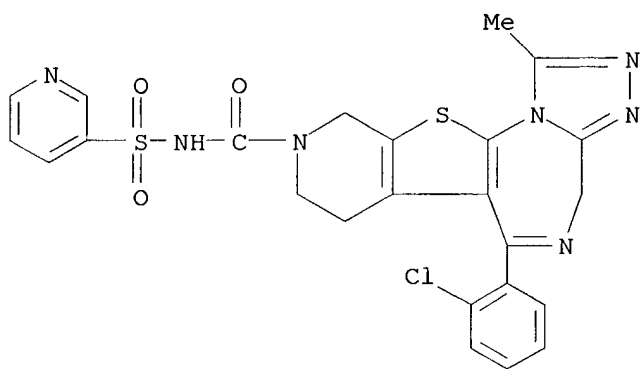
RN 132442-67-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)

09/701,893



RN 138192-67-3 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



09/701,893

~~L2~~ ANSWER 76 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1992:34273 CAPLUS

DN 116:34273

TI Pharmacological effects of oral E6123, a novel PAF antagonist, on biological changes induced by PAF inhalation in guinea pigs

AU Sakuma, Y.; Tsunoda, H.; Shirato, M.; Katayama, S.; Yamatsu, I.; Katayama, K.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300, Japan

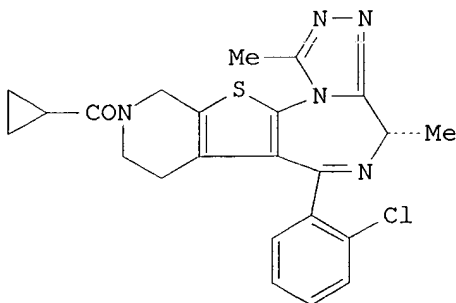
SO Prostaglandins (1991), 42(5), 463-72

CODEN: PRGLBA; ISSN: 0090-6980

DT Journal

LA English

GI



I

AB The effects of a newly synthesized PAF antagonist E6123 (I) on in vivo inhaled PAF-induced pulmonary changes were investigated. E6123 inhibited PAF inhalation-induced bronchoconstriction in guinea pigs with an ED50 value (p.o.) of 1.3 .mu.g/kg which was lower than those of other PAF-antagonists such as WEB2347 (ED50 = 26 .mu.g/kg) and Y-24180 (ED50 = 12 .mu.g/kg). E6123 significantly inhibited PAF inhalation-induced eosinophil infiltration into the bronchiole and trachea, and bronchial hyperreactivity in guinea pigs after oral administration at 1 and 10 .mu.g/kg, resp. E6123 inhibited the PAF-induced increase in intracellular free calcium ion concn. ([Ca2+]i) in guinea pig eosinophils with an IC50 value of 14 nM. The present results suggest that E6123 may be beneficial for the treatment of asthma, in which PAF is assumed to be involved.

IT 131614-02-3, E 6123

RL: BIOL (Biological study)

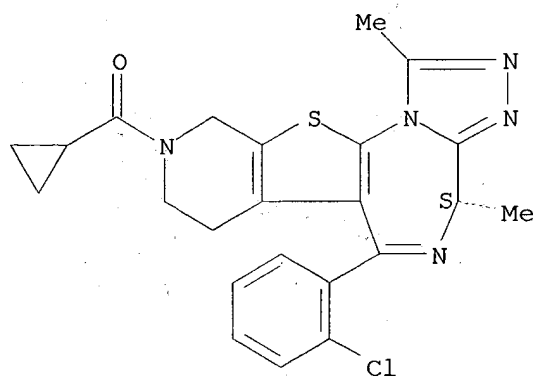
(platelet-activating factor-induced bronchoconstriction and eosinophil infiltration and bronchial hyperreactivity inhibition by, antiasthmatic action in relation to)

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/701,893



09/701,893

~~123~~ ANSWER 77 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1992:34259 CAPLUS

~~DN~~ 116:34259

~~TI~~ Pharmacological activities of a novel thienodiazepine derivative as a platelet-activating factor antagonist. Effects on microvascular permeability, hypotension and nephrosis

~~AU~~ Sakuma, Y.; Shirato, M.; Nagaoka, J.; Obaishi, H.; Tsunoda, H.; Katayama, S.; Ono, H.; Katayama, K.

~~CS~~ Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

~~SO~~ Arzneim.-Forsch. (1991), 41(12), 1255-9

CODEN: ARZNAD; ISSN: 0004-4172

~~DT~~ Journal

~~LA~~ English

~~AB~~ The effects of a newly synthesized platelet-activating factor (PAF) antagonist, (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,3]triazolo[4,3-a][1,4]diazepine (E-6123) on microvascular permeability, systemic hypotension and nephrosis were investigated. E-6123 inhibited PAF injection-induced microvascular permeability (edema) in guinea pigs after oral administration at 3 .mu.g/kg. The inhibitory effects of E-6123 were very potent compared to those of other PAF antagonists. E-6123 reversed PAF and/or endotoxin injection-induced hypotension in rats after i.v. administration at 3 .mu.g/kg. The increase in urinary protein excretion of rats in which nephrosis had been induced by i.p. injection of aminonucleoside was not inhibited by oral administration of E-6123 at 10 mg/kg/day.

~~IT~~ 131614-02-3, E-6123

RL: BAC (Biological activity or effector, except adverse); THU

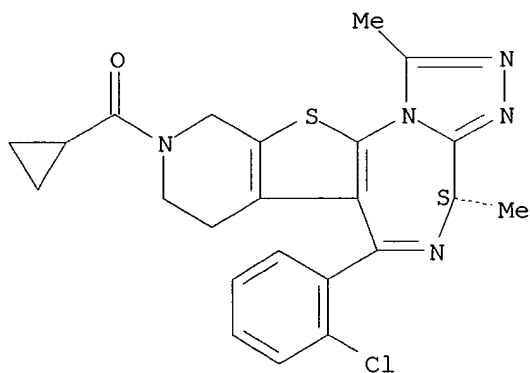
(Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacol. of, as platelet-activating factor antagonist)

~~RN~~ 131614-02-3 CAPLUS

~~CN~~ 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/701,893

~~IN~~ 23 ANSWER 78 OF 92 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1991:680072 CAPLUS

DN 115:280072

TI Preparation of 6-(2-chlorophenyl)-9-carbamoyl-7,8,9,10-tetrahydro-1-methyl-4H-pyrido[4',3':4,5]thieno[3,2-f]1,2,4-triazolo[4,3-a]-1,4-diazepines as PAF antagonists

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Rolland, Alain

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Ger. Offen., 13 pp.

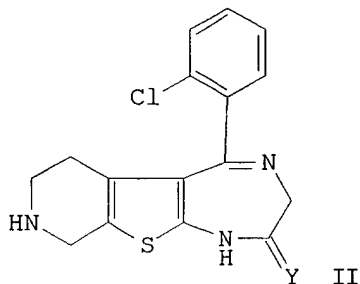
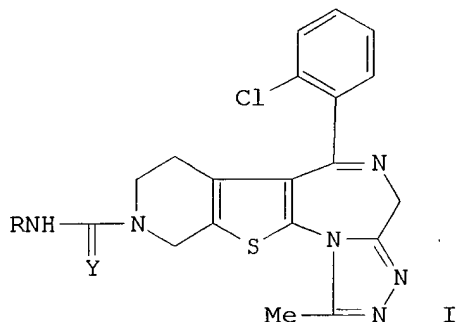
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4010315	A1	19911002	DE 1990-4010315	19900330
OS	MARPAT 115:280072				
GI					



AB Title compds. [I; Y = O, S; R = (cyclo)alkyl, alkenyl, (hetero)arylalkyl, (substituted) Ph, heteroatom-contg. condensed bicyclic residue, phenylsulfonyl, heteroarylsulfonyl, bicyclicsulfonyl], were prepd. by 1) acylation of thienotriazolodiazepines II with excess RNCY, 2) condensation of the product with excess N₂H₄, and 3) cyclocondensation of the hydrazine with 4 equiv. (EtO)₃CMe. Thus, II (Y = S) (prepn. starting from NCCH₂CO₂H and 2-ClC₆H₄COCl given), in MeOH was treated with 4-MeOC₆H₄NCS followed by 2 h reflux to give 83% 8-thiocarbamoyl deriv. This in THF was treated with N₂H₄.cntdot.H₂O to give 86% 2-hydrazone which was refluxed with (EtO)₃CMe in EtOH to give 92% I (R = 4-MeOC₆H₄, Y = S) (III). The latter gave 83.5% inhibition of PAF-induced bronchoconstriction in guinea pigs.

IT **132418-36-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)

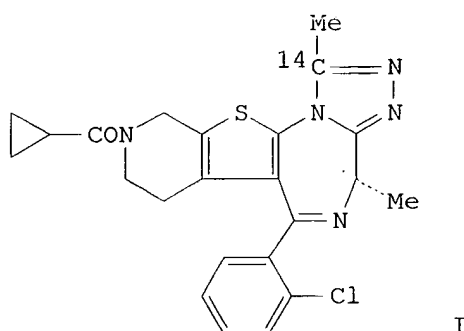
(prepn. of, from pyridothienodiazepinethione deriv.)

RN 132418-36-1 CAPLUS

see 75892

09/701,893

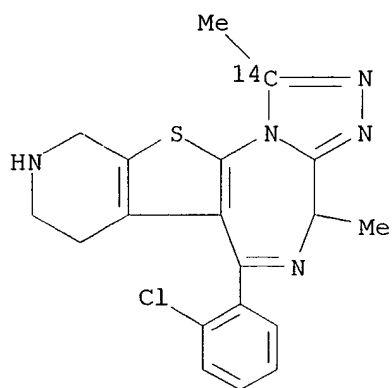
~~E23~~ ANSWER 79 OF 92 CAPLUS COPYRIGHT 2001 ACS
~~AN~~ 1991:679973 CAPLUS
~~DN~~ 115:279973
TI Synthesis of 14C-labeled (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-
8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-
f][1,2,4]triazolo[4,3-a][1,4]diazepine (14C-E6123)
AU Miyazawa, Shuhei; Okano, Kazuo; Kusano, Kazutomi; Tadano, Kyoichi; Tanaka,
Shigeru; Yuzuriha, Teruaki; Machida, Yoshimasa; Yamatsu, Isao
CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan
SO J. Labelled Compd. Radiopharm. (1991), 29(9), 1073-7
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
GI



AB The title compd. (I), a platelet activating factor receptor antagonist for
studying the pharmacokinetic profile of E6123, was synthesized in three
steps using [1-14C] acetyl hydrazine fumarate as the labeled starting
material. The final product has high chem. and radiochem. purity with a
specific activity of 53.2mCi per mmol (1.97GBq per mmol). The overall
radiochem. yield is 6.0%.

IT **137503-67-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation of, by cyclopropanecarbonyl chloride)

RN 137503-67-4 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-1-
14C, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX
NAME)

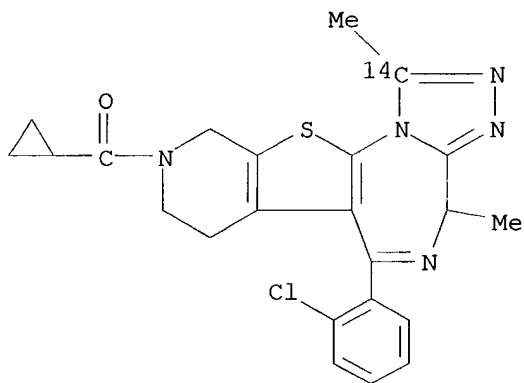


IT **137503-68-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resoln. of)

RN 137503-68-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-1-
14C, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl- (9CI) (CA INDEX NAME)



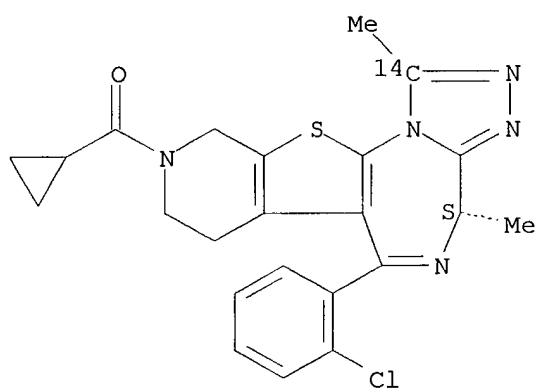
IT **137567-98-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 137567-98-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-1-
14C, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/701,893

E23 ANSWER 80 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:526758 CAPLUS

DN 115:126758

TI Effects of a novel PAF antagonist, E6123, on passive anaphylaxis

AU Sakuma, Y.; Tsunoda, H.; Katayama, S.; Harada, K.; Obaishi, H.; Shirato, M.; Yamada, K.; Miyazawa, S.; Okano, K.; et al.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SO Agents Actions Suppl. (1990), 31(Mediators Airway Hyperreact.), 255-8
CODEN: AASUDJ; ISSN: 0379-0363

DT Journal

LA English

AB E6123 inhibited antigen-induced bronchoconstriction, the development of bronchial hyperreactivity and eosinophil infiltration in the airway in passively sensitized guinea pigs and protected mice from anaphylactic death. The inhibitory effects of E6123 on the anaphylactic response were very potent compared with those of WEB 2347 and Y-24180.

IT 131614-02-3, E6123

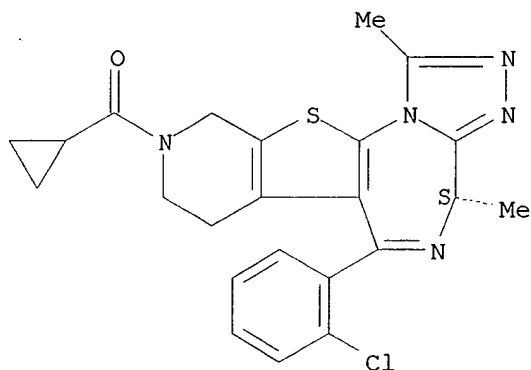
RL: BIOL (Biological study)

(passive anaphylaxis response to, as platelet-activating factor antagonist)

RN 131614-02-3 CAPLUS

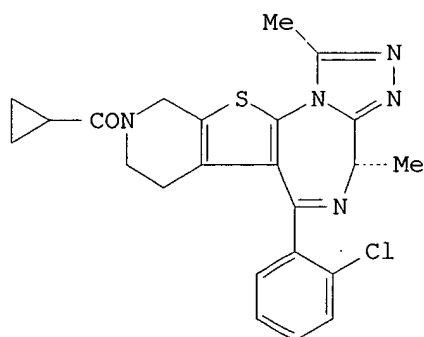
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/701,893

~~123~~ ANSWER 81 OF 92 CAPLUS COPYRIGHT 2001 ACS
~~AN~~ 1991:526757 CAPLUS
~~DN~~ 115:126757
TI Effects of a novel PAF antagonist, E 6123, on PAF-induced biological responses
AU Tsunoda, H.; Sakuma, Y.; Harada, K.; Muramoto, K.; Katayama, S.; Horie, T.; Shimomura, N.; Clark, R.; Miyazawa, S.; et al.
CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan
SO Agents Actions Suppl. (1990), 31(Mediators Airway Hyperreact.), 251-4
CODEN: AASUDJ; ISSN: 0379-0363
DT Journal
LA English
GI



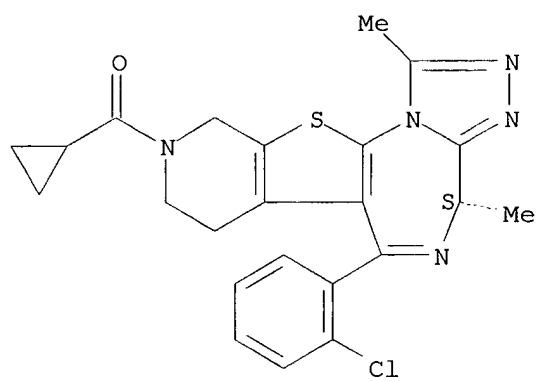
AB E 6123 (I) is a new member of the benzodiazepine class of PAF antagonists. Although I has similar activity in vitro to the 2 representative antagonists WEB 2347 and Y 24180, in vivo it is far more active than these compds. Thus, I was effective in inhibiting dose-dependently PAF-induced bronchoconstriction when administered orally or i.v. (IC₅₀ 1.0 and 1.3 .mu.g/Kg, resp., at 3 h), and had a min. ED of 10 .mu.g/Kg and 3 .mu.g/Kg, resp., against PAF-induced hematoconcn. and edema at 3 h after oral administration. Furthermore, I protects mice from PAF-induced death dose-dependently (ED₅₀ 7 .mu.g/Kg at 3 h). I should prove valuable in pharmacol. and clin. research in the roles of PAF, and in therapy of diseases such as asthma, in which PAF is assumed to play a pathol. role.

IT **131614-02-3**, E6123
RL: BIOL (Biological study)
(as platelet-activating factor antagonist)

RN 131614-02-3 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

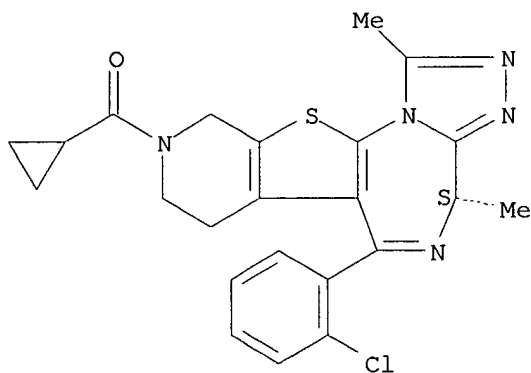
Absolute stereochemistry.

09/701,893



123 ANSWER 82 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1991:240355 CAPLUS
 DN 114:240355
 TI Activity of a novel thienodiazepine derivative as a platelet-activating factor antagonist in guinea pig lungs: effects on platelet-activating factor and allergen induced eosinophil accumulation
 AU Tsunoda, H.; Sakuma, Y.; Shirato, M.; Obaishi, H.; Harada, K.; Yamada, K.; Shimomura, N.; Machida, Y.; Yamatsu, I.; Katayama, K.
 CS Allergy Asthma Res. Unit, Eisai Co., Ltd., Ibaraki, 300-26, Japan
 SO Arzneim.-Forsch. (1991), 41(3), 224-7
 CODEN: ARZNAD; ISSN: 0004-4172
 DT Journal
 LA English
 AB Platelet-activating factor (PAF) inhalation in guinea pigs caused a significant increase in the no. of eosinophils recovered from bronchoalveolar lavage fluid (BALF). Oral administration of (S)-(+)-6-(2-chlorophenyl)-3-cyclopropanecarbonyl-8,11-dimethyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine (E-6123), a novel PAF antagonist, at the dose of 100 .mu.g/kg completely inhibited the PAF-induced eosinophil accumulation. Antigen inhalation in passively sensitized guinea pigs caused a significant increase in lung contents of PAF at 5 min, and accumulation of eosinophils in the bronchi 1 and 2 days thereafter. E-6123 inhibited the antigen-induced eosinophil accumulation and the max. inhibition was approx. 65%. On the other hand, methylprednisolone completely inhibited the antigen-induced eosinophil accumulation. The results suggest that PAF is a potent attractant of eosinophils and is involved in antigen-induced eosinophil infiltration into bronchi. The results also suggest that E-6123 may be of therapeutic value in the treatment of asthma exhibiting eosinophil recruitment in airways.
 IT 131614-02-3, E-6123
 RL: BIOL (Biological study)
 (as platelet-activating factor antagonist, asthma treatment with, eosinophils in)
 RN 131614-02-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 83 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:240237 CAPLUS

DN 114:240237

TI Inhibitory effect of new PAF antagonists on PAF-induced rabbit platelet aggregation in vitro and ex vivo

AU Yue, Tian Li; Rabinovici, Reuven; Farhat, Michel; Feuerstein, Giora

CS Dep. Pharmacol., SmithKline Beecham, King of Prussia, PA, 19406-0939, USA

SO J. Lipid Mediators (1991), 3(1), 13-26

CODEN: JLMEEG; ISSN: 0921-8319

DT Journal

LA English

AB The effect of BN 50739, a recently developed PAF antagonist, on PAF-induced rabbit platelet aggregation in vitro and ex vivo was investigated. BN 50739 caused a right shift in PAF dose-response curves of platelet aggregation both in vitro and ex vivo. The amplitude of max. aggregation, however, did not change as the concn. of PAF was increased indicating that BN 50739 is a competitive inhibitor. In vitro, in the presence of 10, 33, and 66 nM BN 50739, the EC50 of PAF-inducing aggregation increased 3.7, 11.1, and 50 times, resp., and platelet disaggregation was promoted. The IC50 of BN 50739 for 2.5 nM PAF-inducing platelet aggregation was 13.8 nM. Under the same condition, the IC50s of BN 50741, BN 50730, BN 50726, SRI 63-441, and BN 52021 were 18.3, 33.1, 63.4, 712, and 24,600 nM, resp. BN 50739 given i.p. at 1, 3, or 10 mg/kg increased the concn. of PAF inducing 50% max. platelet-rich plasma aggregation 3.4, 28, and 134 times, resp. The apparent biol. half-life of BN 50739 at 3 and 10 mg/kg i.p. was 2.5 and 5.4 h, resp. BN 50739 had no effect on arachidonic acid (AA)- or collagen-induced platelet aggregation at concns. effectively inhibiting PAF-induced platelet aggregation; however, moderate inhibition on AA- and collagen-induced aggregation was obsd. as the concn. of BN 50739 exceeded 100 nM. The results indicate that BN 50739 is the most potent and competitive PAF antagonist.

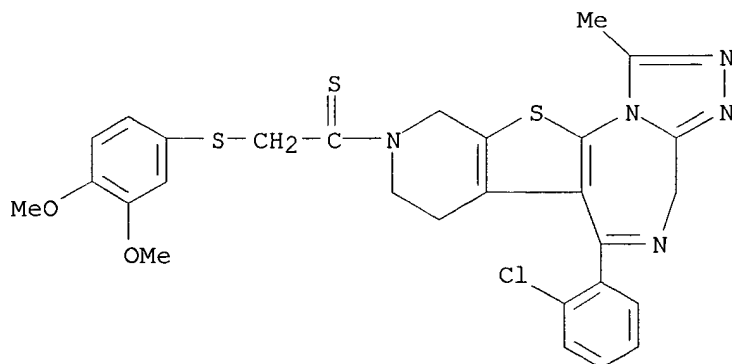
IT 128672-07-1, BN 50739 132579-32-9, BN 50730

RL: BIOL (Biological study)

(as platelet-activating factor antagonist, PAF-induced platelet aggregation inhibition by)

RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

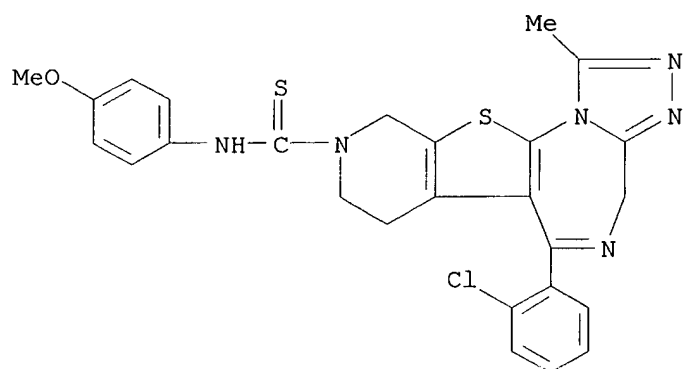


RN 132579-32-9 CAPLUS

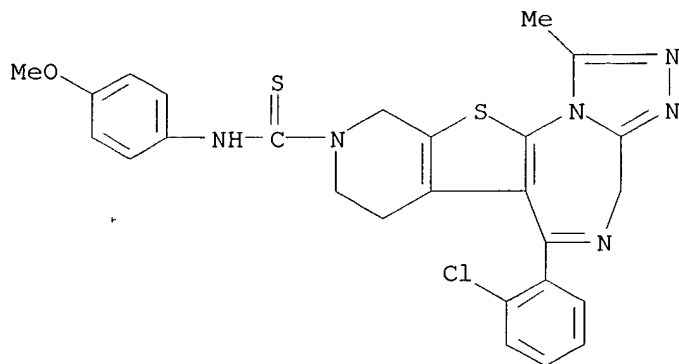
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-

09/701,893

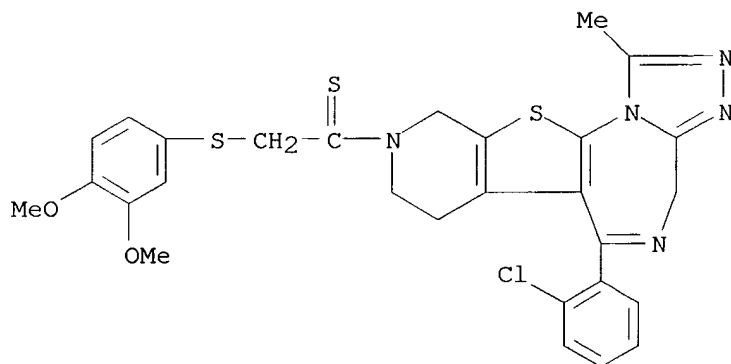
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 84 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1991:221121 CAPLUS
DN 114:221121
TI Allergen-induced bronchospasm in passively sensitized guinea pigs:
influence of new substances in comparison to reference compounds
AU Madi, Sawsan; Giessler, J.; Hirschelmann, R.; Friedrich, G.; Braquet, P.
CS Sekt. Pharm., Martin-Luther-Univ. Halle-Wittenberg, Halle/Saale, O-4010,
Fed. Rep. Ger.
SO Agents Actions (1991), 32(1-2), 144-5
CODEN: AGACBH; ISSN: 0065-4299
DT Journal
LA English
AB The new phospholipase A2 inhibitor 3-(4-octadecyl)benzoylacrylic acid and
the blood platelet activating factor antagonist BN-50730 were compared for
bronchospasmolytic activity with several bronchodilators and
antiasthmatics. The assays were done on ovalbumin-sensitized guinea pigs.
BN-50730 had clear antiasthmatic effects. These effects may be enhanced
in combination with the benzoylacrylic acid deriv.
IT **132579-32-9**, BN-50730
RL: PRP (Properties)
(bronchodilatory effects of)
RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
1-methyl- (9CI) (CA INDEX NAME)

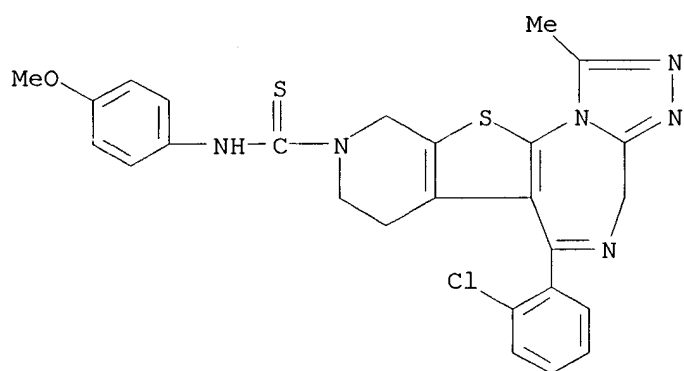


L23 ANSWER 85 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1991:198909 CAPLUS
 DN 114:198909
 TI New trends in PAF antagonist research: a new series of potent
 hetrapazine-derived PAF antagonists
 AU Braquet, P.; Esanu, A.
 CS Inst. Henri Beaufour, Le Plessis-Robinson, 92350, Fr.
 SO Agents Actions (1991), 32(1-2), 34-6
 CODEN: AGACBH; ISSN: 0065-4299
 DT Journal; General Review
 LA English
 AB A review with 6 refs. on a new series of platelet-activating factor (PAF)
 antagonists related to the structure of the WEB 2086 and other
 triazolo-thenodiazepines. Four of these compds., BN 50726, 50727, BN
 50730, and BN 50739 have been selected for further development and this
 paper describes their pharmacol.
 IT **128672-07-1**, BN 50739 **132579-32-9**, BN 50730
133686-55-2, BN 50727
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmacol. of, platelet-activating factor antagonism in)
 RN 128672-07-1 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-
 7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132579-32-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
 9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-
 1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 133686-55-2 CAPLUS

09/701,893

L23 ANSWER 86 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:122433 CAPLUS

DN 114:122433

TI Preparation of 9-alkylthiomethylcarbonyl-7,8,9,10-tetrahydro-1-methyl-4H-pyrido[4',3':4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]-1,4-diazepines as antiischemics and blood platelet aggregation inhibitors

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Pommier, Jacques

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Ger. Offen., 13 pp.

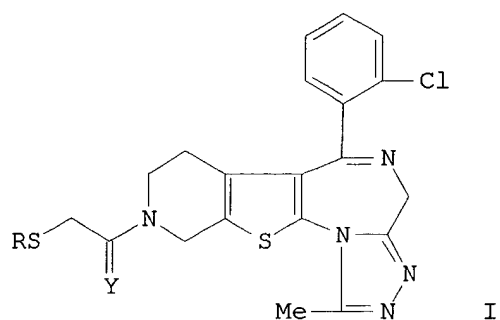
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

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	NO 9001813	A	19901114	NO 1990-1813	19900424
	NO 173607	B	19930927		
	NO 173607	C	19940105		
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	AT 9000957	A	19911015		
	DK 9001029	A	19901114	DK 1990-1029	19900426
	ZA 9003305	A	19910227	ZA 1990-3305	19900430
	ZA 9003304	A	19910227	ZA 1990-3304	19900430
	CH 681009	A	19921231	CH 1990-1522	19900504
	NL 9001089	A	19901203	NL 1990-1089	19900507
	BE 1004122	A3	19920929	BE 1990-479	19900507
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	SE 505407	C2	19970825	SE 1990-1670	19900509
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	AU 9054931	A1	19901115	AU 1990-54931	19900511
	AU 628171	B2	19920910		
	FR 2646774	A1	19901116	FR 1990-5880	19900511
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	ES 2019840	A6	19910701	ES 1990-1320	19900511
	US 5049559	A	19910917	US 1990-522235	19900511
	AU 620513	B2	19920220	AU 1990-54930	19900511
	AU 9054930	A1	19911205		
	FI 93119	B	19941115	FI 1990-2355	19900511
	FI 93119	C	19950227		
PRAI	GB 1989-11030		19890513		
OS	CASREACT 114:122433; MARPAT 114:122433				
GI					



AB The title compds. [I; R = alkyl, (substituted) Ph, furyl, thienyl; Y = O, S], were prepd. Thus, a mixt. of N-carboethoxy-4-piperidone, S, 2-ClC₆H₄COCH₂CN (prepn. given), morpholine, and MeOH was refluxed 1 h to give 2-amino-3-(2-chlorobenzoyl)-6-(ethoxycarbonyl)-4,5,6,7-tetrahydropyrido[3,4-b]thiophene. This was successively acylated with BrCH₂COBr, amidated with NH₃, and refluxed in pyridine to give 5-(2-chlorophenyl)-8-(ethoxycarbonyl)-6,7,8,9-tetrahydro-3H-pyrido[4',3':4,5]thieno[3,2-f]-1,4-diazepin-2-one. The latter was converted to I (R = Me₂CH, Y = O) in several steps. I inhibited platelet activating factor-induced platelet aggregation with IC₅₀ of 6.36 .times. 10⁻⁹ to 5.11 .times. 10⁻⁷ M.

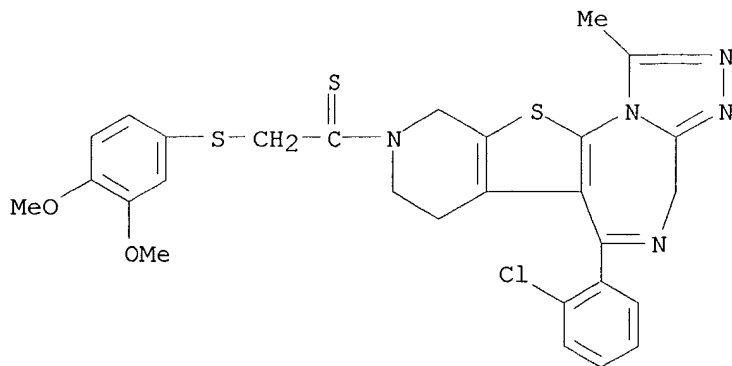
IT 128672-07-1P 132522-27-1P 132522-28-2P
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 132522-35-1P 132522-36-2P 132522-37-3P
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 132522-53-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as antiischemic and blood platelet aggregation inhibitor)

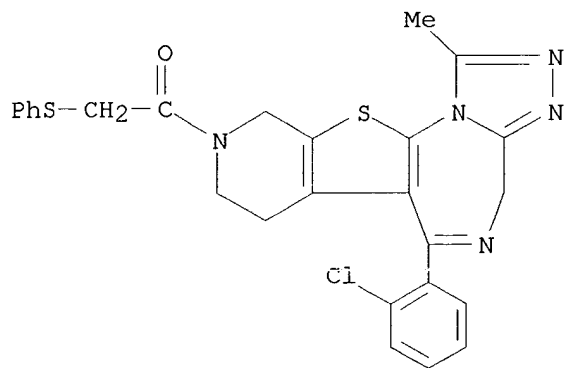
RN 128672-07-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-[2-[(3,4-dimethoxyphenyl)thio]-1-thioxoethyl]-
 7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



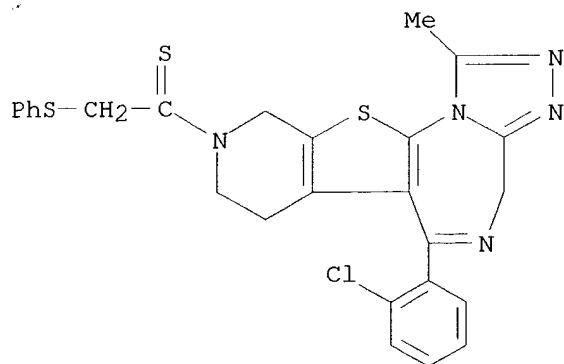
RN 132522-27-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(phenylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-28-2 CAPLUS

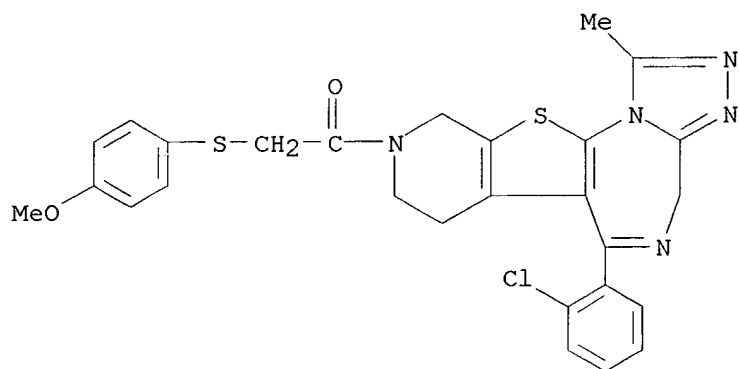
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(phenylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)



RN 132522-29-3 CAPLUS

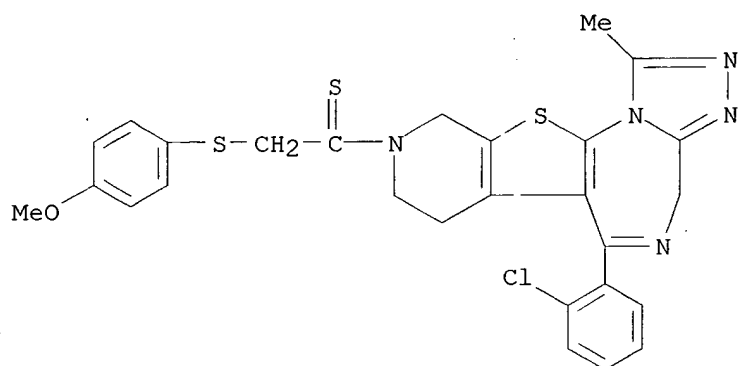
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[[4-methoxyphenyl]thio]acetyl]-1-
methyl- (9CI) (CA INDEX NAME)

09/701,893



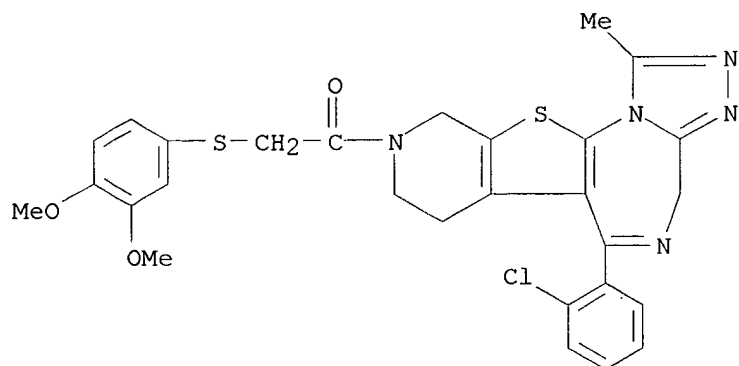
RN 132522-30-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-[2-[(4-methoxyphenyl)thio]-1-
thioxoethyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-31-7 CAPLUS

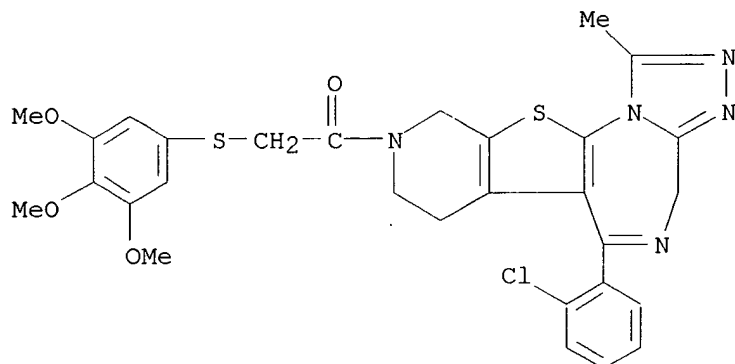
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[3,4-dimethoxyphenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



09/701,893

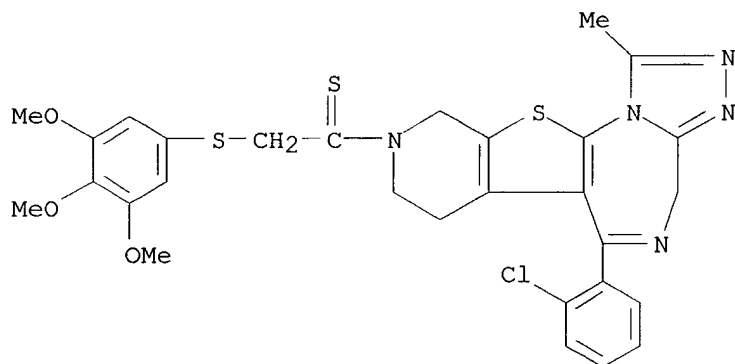
RN 132522-32-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(3,4,5-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



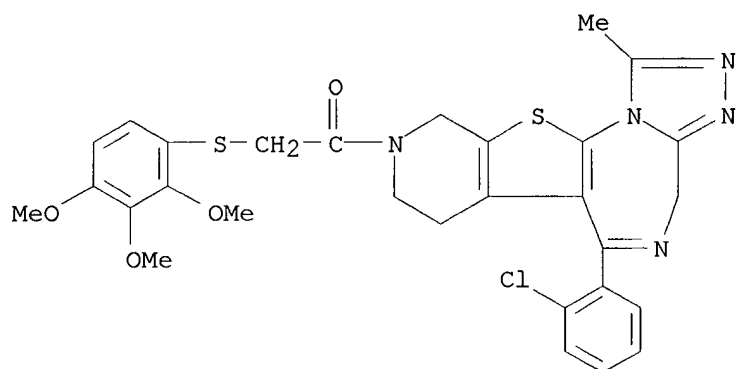
RN 132522-33-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(3,4,5-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



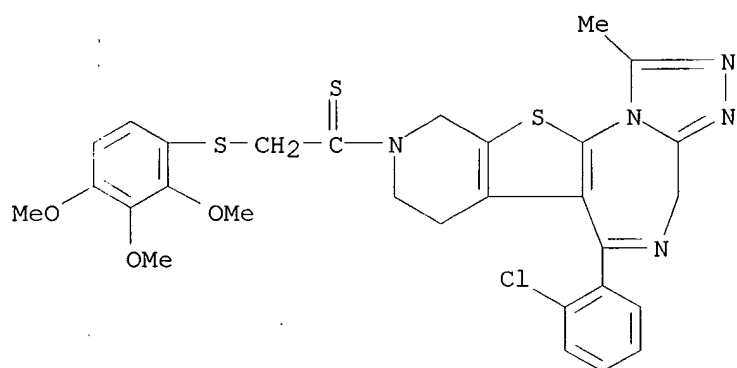
RN 132522-34-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[(2,3,4-
trimethoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



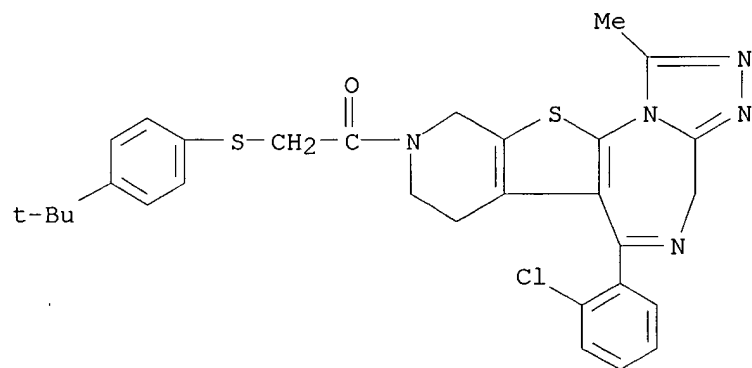
RN 132522-35-1 CAPLUS

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6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[(2,3,4-
trimethoxyphenyl)thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-36-2 CAPLUS

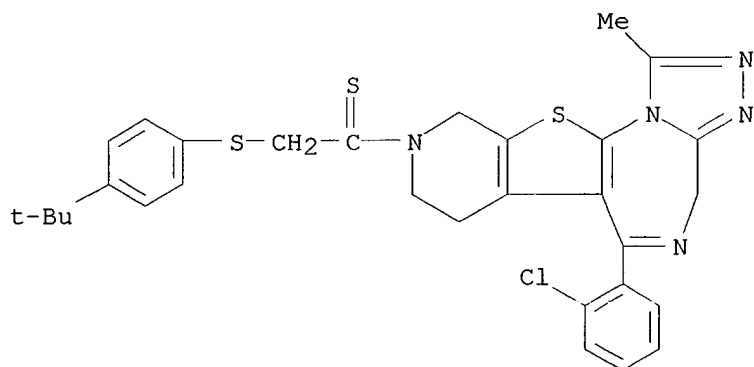
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[[[4-(1,1-dimethylethyl)phenyl]thio]acetyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



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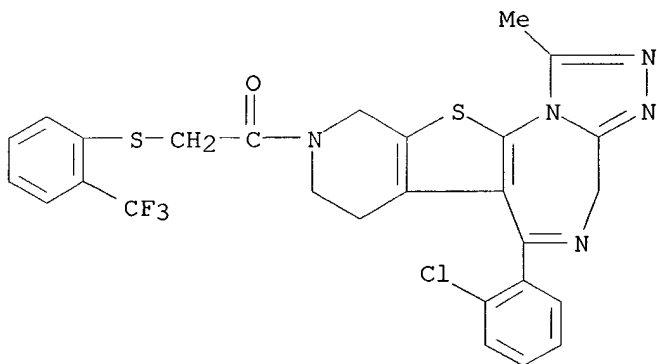
RN 132522-37-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[[4-(1,1-dimethylethyl)phenyl]thio]-1-thioxoethyl]-
7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



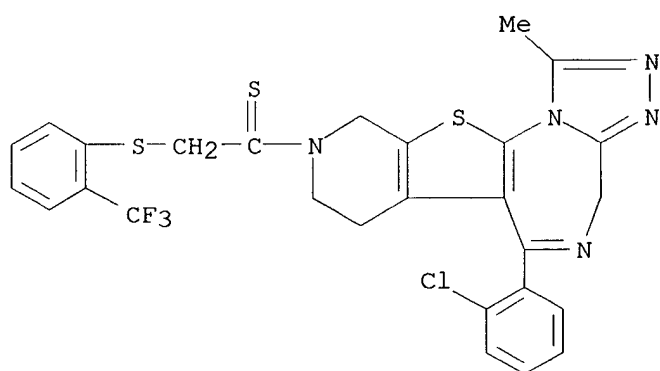
RN 132522-38-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[2-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)

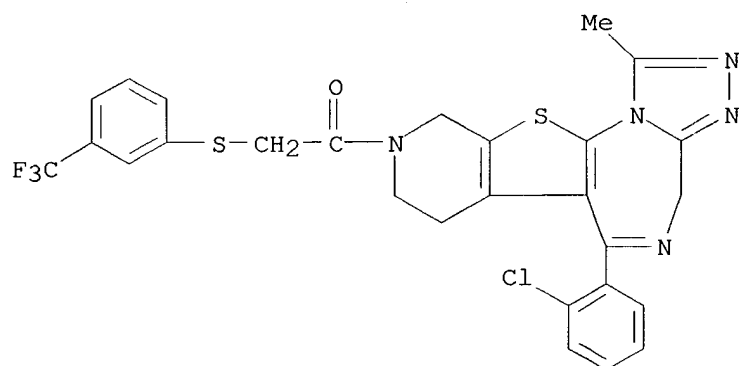


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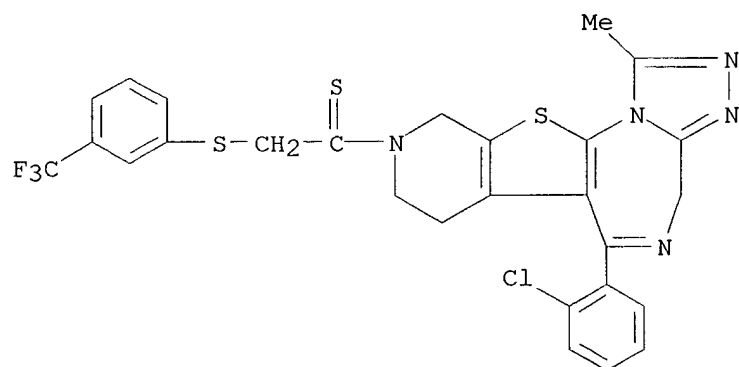
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6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[2-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-40-8 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[[3-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



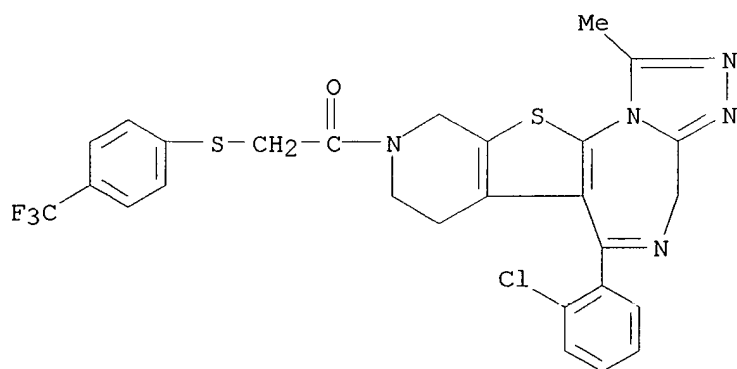
RN 132522-41-9 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[3-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



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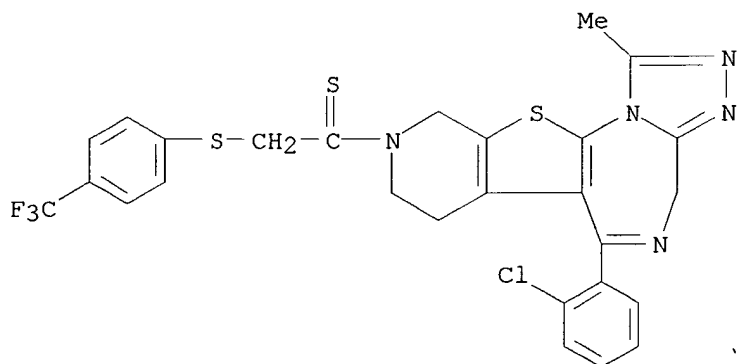
RN 132522-42-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[[4-(trifluoromethyl)phenyl]thio]acetyl]- (9CI) (CA INDEX NAME)



RN 132522-43-1 CAPLUS

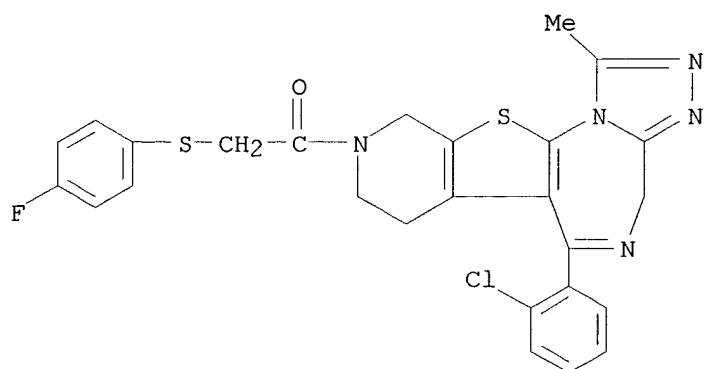
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6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-thioxo-2-[[4-(trifluoromethyl)phenyl]thio]ethyl]- (9CI) (CA INDEX NAME)



RN 132522-44-2 CAPLUS

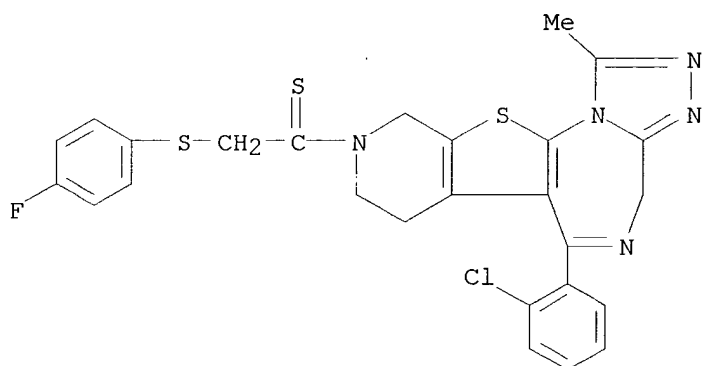
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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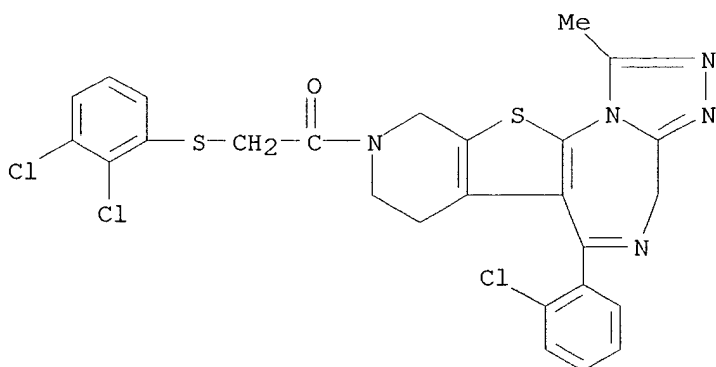
RN 132522-45-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[2-[(4-fluorophenyl)thio]-1-thioxoethyl]-7,8,9,10-
tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132522-46-4 CAPLUS

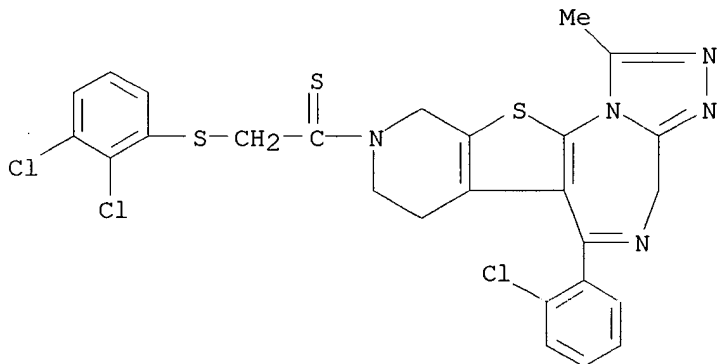
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



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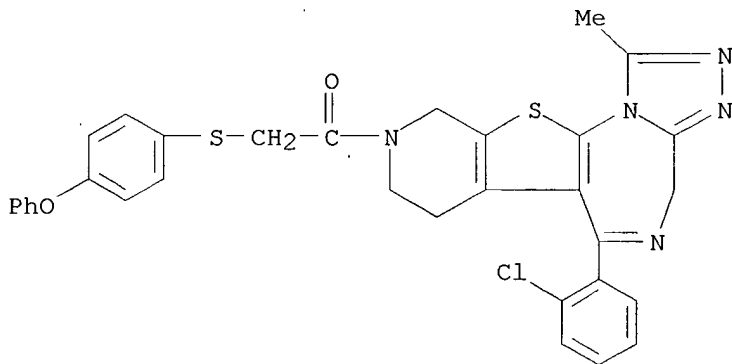
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CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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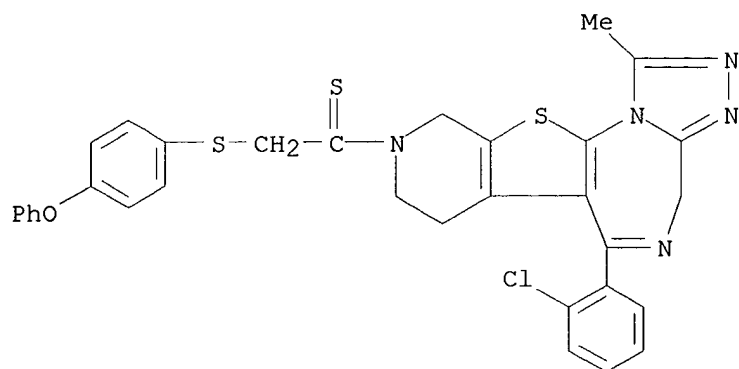
RN 132522-48-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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phenoxyphenyl)thio]acetyl]- (9CI) (CA INDEX NAME)



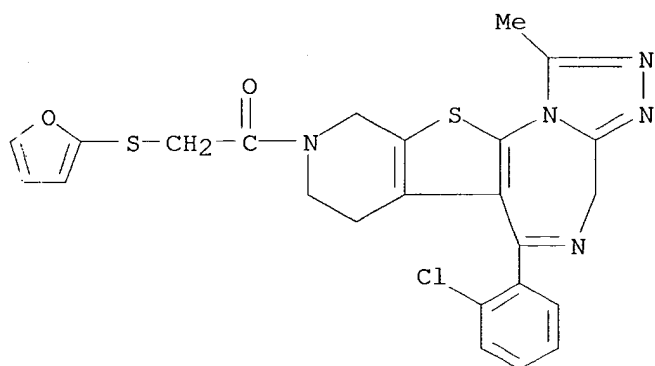
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CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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phenoxyphenyl)thio]-1-thioxoethyl]- (9CI) (CA INDEX NAME)



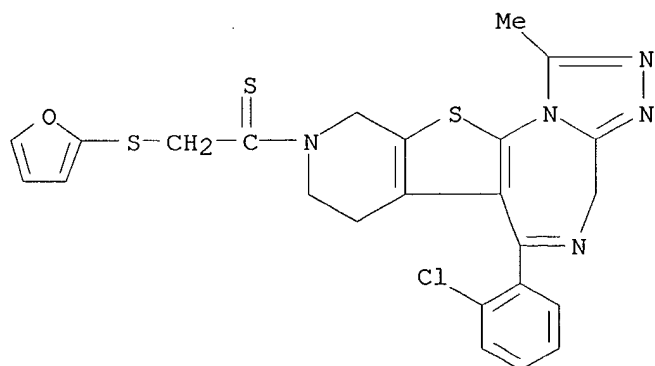
RN 132522-50-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(2-furanylthio)acetyl]-7,8,9,10-tetrahydro-1-methyl-
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RN 132522-51-1 CAPLUS

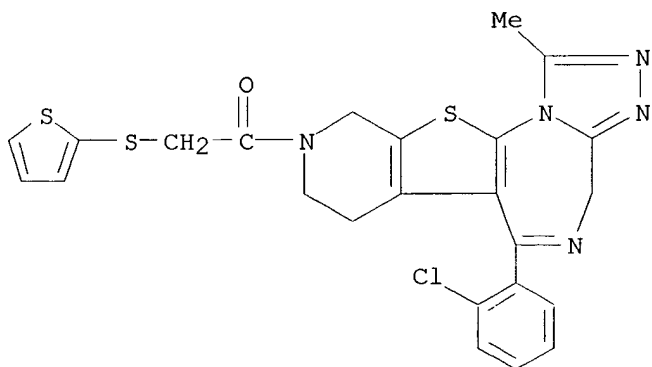
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
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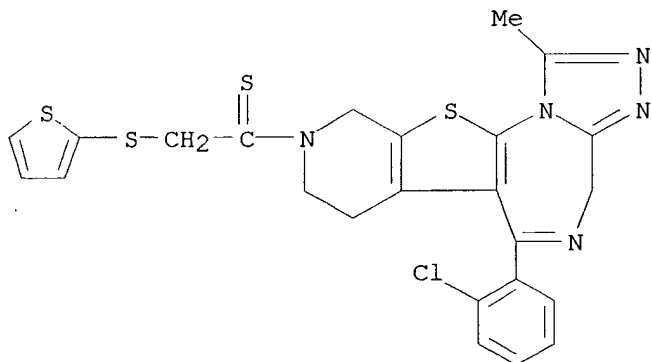
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6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-thienylthio)acetyl]-
(9CI) (CA INDEX NAME)



RN 132522-53-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[2-(2-thienylthio)-1-
thioxoethyl]- (9CI) (CA INDEX NAME)



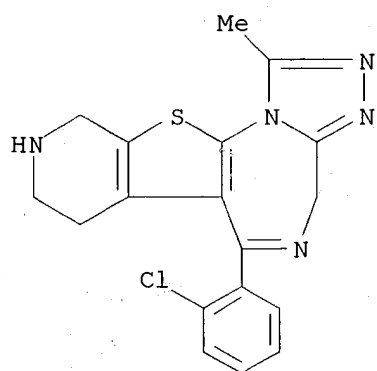
IT 114800-58-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antiischemic and blood platelet
aggregation inhibitor)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



9

L23 ANSWER 87 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:122431 CAPLUS

DN 114:122431

TI Preparation of 7,8,9,10-tetrahydropyrido[4',3':4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]-1,4-diazepines as platelet activating factor (PAF) antagonists

IN Braquet, Pierre; Esanu, Andre; Laurent, Jean Pierre; Rolland, Alain

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Ger. Offen., 12 pp.

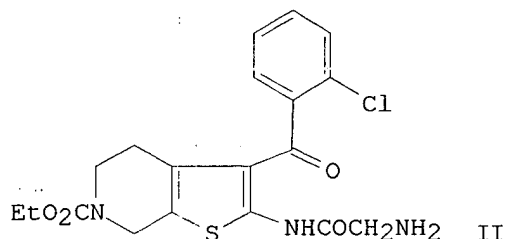
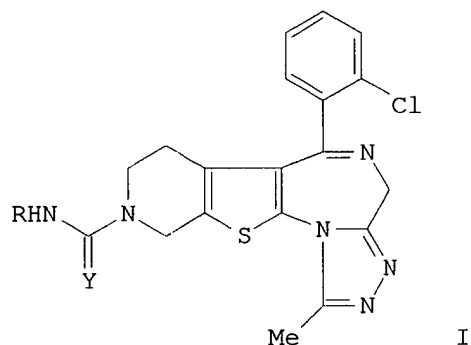
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

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PI	DE 4010316	A1	19901004	DE 1990-4010316	19900330
	NO 9001070	A	19901001	NO 1990-1070	19900307
	NO 173784	B	19931025		
	NO 173784	C	19940202		
	ZA 9001765	A	19901228	ZA 1990-1765	19900307
	ZA 9001763	A	19901228	ZA 1990-1763	19900307
	AT 9000567	A	19911015	AT 1990-567	19900309
	AT 394561	B	19920511		
	AT 394562	B	19920511	AT 1990-568	19900309
	AT 9000568	A	19911015		
	SE 9000871	A	19901001	SE 1990-871	19900312
	SE 505417	C2	19970825		
	NL 9000626	A	19901016	NL 1990-626	19900319
	JP 02289582	A2	19901129	JP 1990-73582	19900326
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	BE 1003699	A3	19920526	BE 1990-343	19900327
	GB 2229723	A1	19901003	GB 1990-7000	19900329
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	CH 680365	A	19920814	CH 1990-1044	19900329
	CA 2013518	AA	19900930	CA 1990-2013518	19900330
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	AU 9052425	A1	19901101	AU 1990-52425	19900330
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	FI 95036	B	19950831	FI 1990-1605	19900330
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	FR 2645022	A1	19901005	FR 1990-4155	19900402
	FR 2645022	B1	19920417		
	FR 2645153	A1	19901005	FR 1990-4156	19900402
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	US 5492906	A	19960220	US 1992-837580	19920218
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GI					



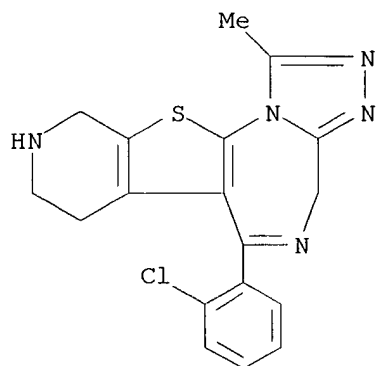
AB The title compds. [I; Y = O, S; R = alkyl, cycloalkyl, alkenyl, (hetero)arylalkyl, (alkyl-, phenyl-, PhO-, alkylsulfonyl-, F-, Cl-, F3C-substituted) Ph, heterobicycclyl, phenylsulfonyl, heteroarylsulfonyl, bicycclylsulfonyl], were prepd. Thus, I (Y = S, R = Me2CH), prepd. in 11 steps from NCCH2CO2H and 2-ClC6H4COCl via thienopiperidine II, gave 90.4% inhibition of PAF-induced bronchospasms in guinea pigs. I showed IC50 of 6.10 .times. 10-9 to 3.66 .times. 10-7 M for inhibition of PAF-induced blood platelet aggregation in rabbits. Most I were nontoxic at 1 g/kg orally or i.p. in mice.

IT **114800-58-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for pyridothienotriazolodiazepine platelet activating factor antagonist)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



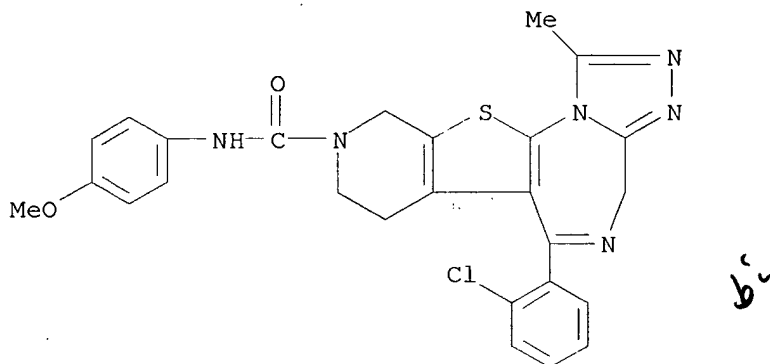
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 132418-50-9P 132418-51-0P 132418-52-1P
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 132418-56-5P 132418-58-7P 132418-59-8P
 132418-60-1P 132418-61-2P 132418-62-3P
 132418-63-4P 132418-64-5P 132442-67-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of, as platelet activating factor antagonist)

RN 132418-35-0 CAPLUS

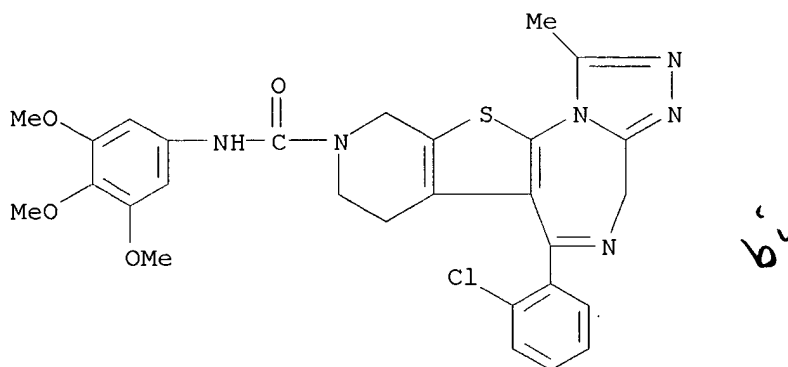
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-36-1 CAPLUS

RN 132418-37-2 CAPLUS

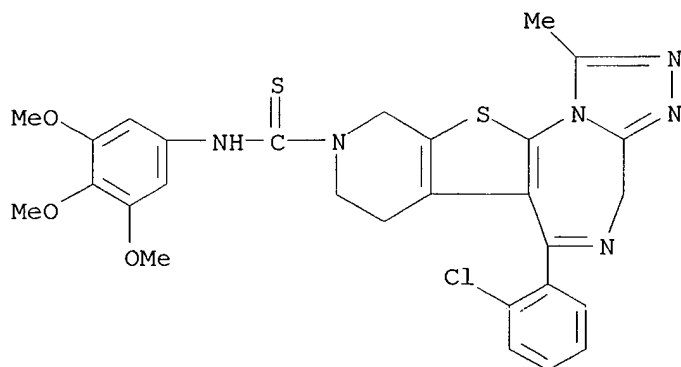
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



09/701,893

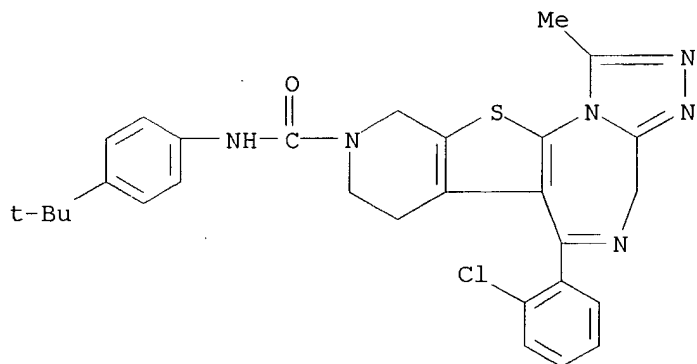
RN 132418-38-3 CAPLUS

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RN 132418-39-4 CAPLUS

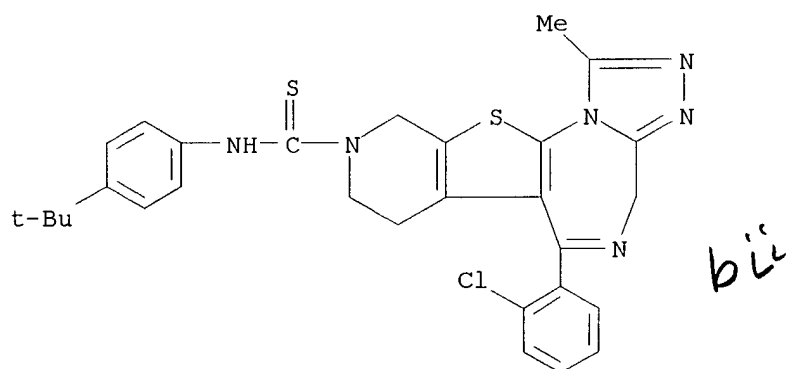
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RN 132418-40-7 CAPLUS

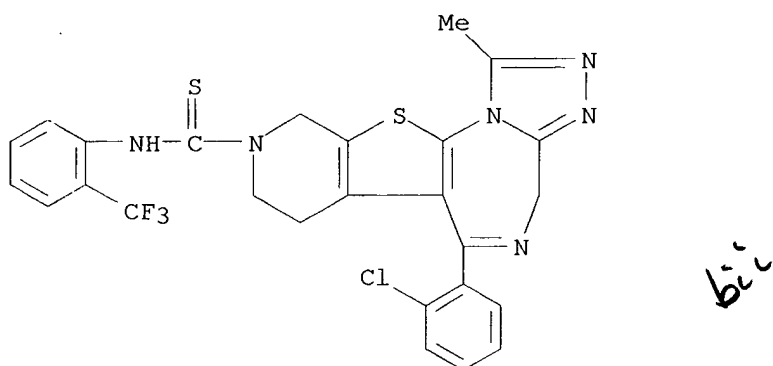
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09/701,893



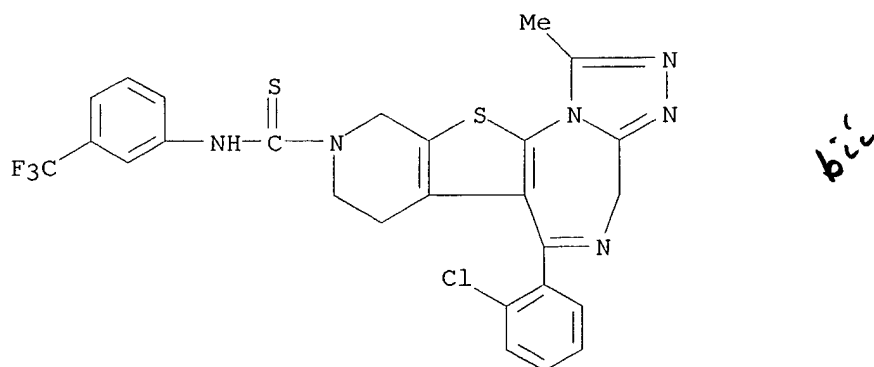
RN 132418-41-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 132418-42-9 CAPLUS

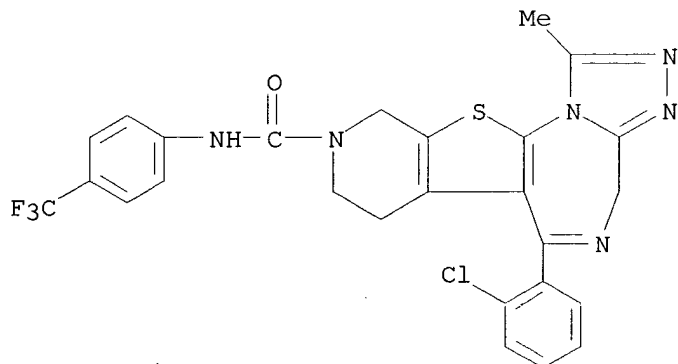
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09/701,893

RN 132418-43-0 CAPLUS

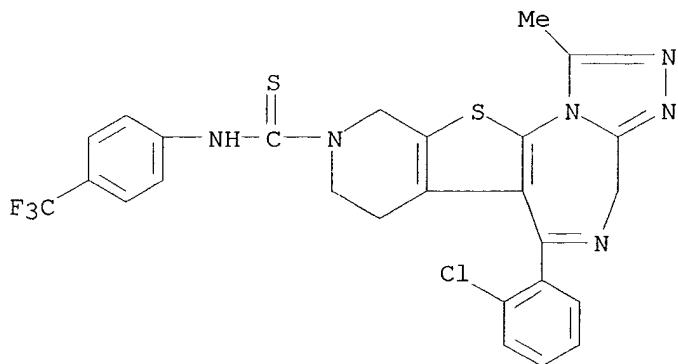
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



b₂

RN 132418-44-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

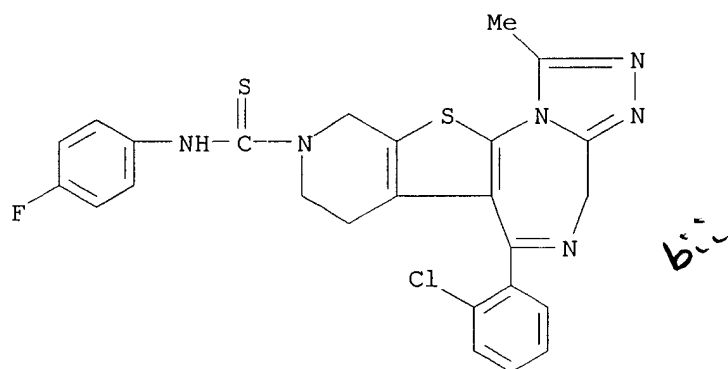


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RN 132418-45-2 CAPLUS

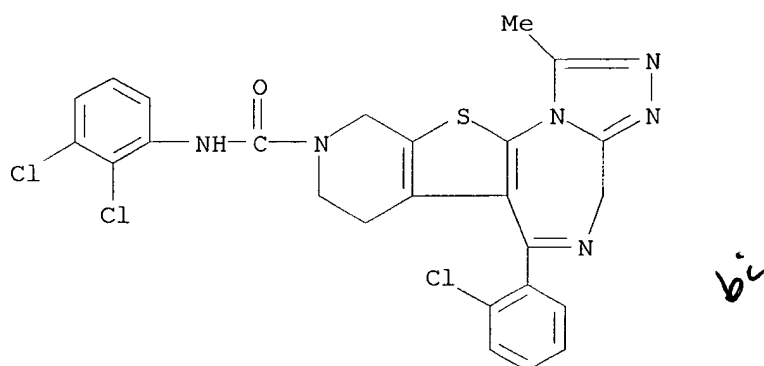
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(4-fluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



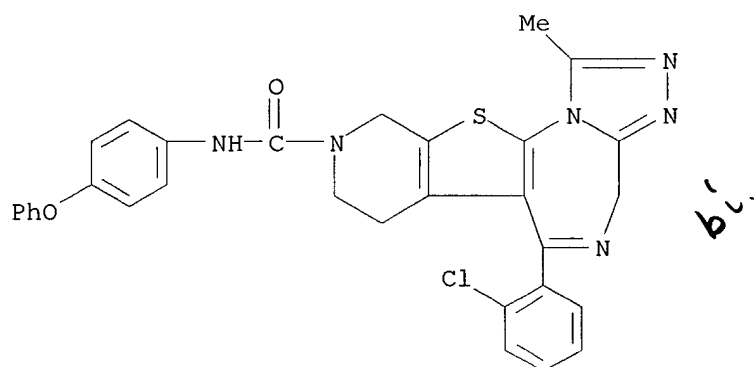
RN 132418-46-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,3-dichlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-47-4 CAPLUS

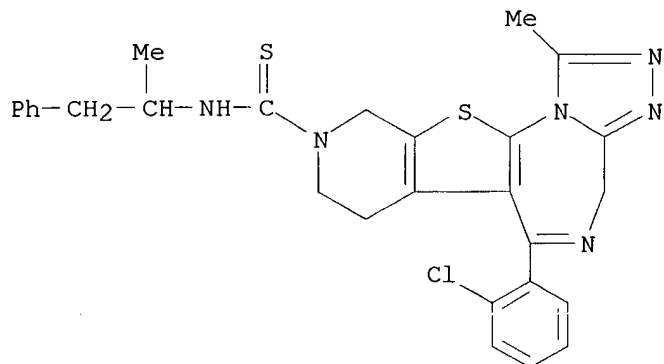
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



09/701,893

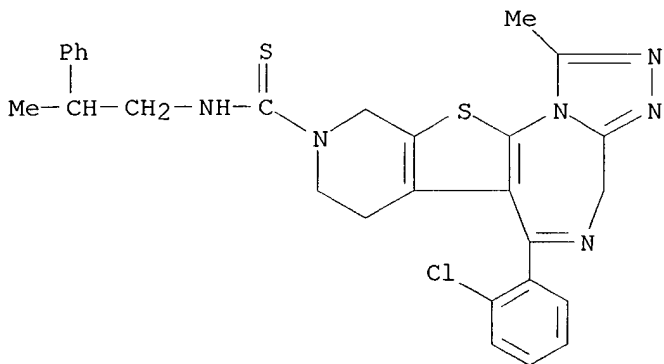
RN 132418-48-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1-methyl-2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 132418-49-6 CAPLUS

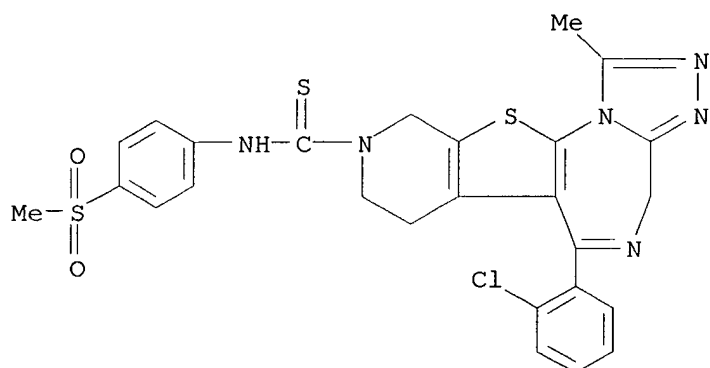
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-phenylpropyl)- (9CI) (CA INDEX NAME)



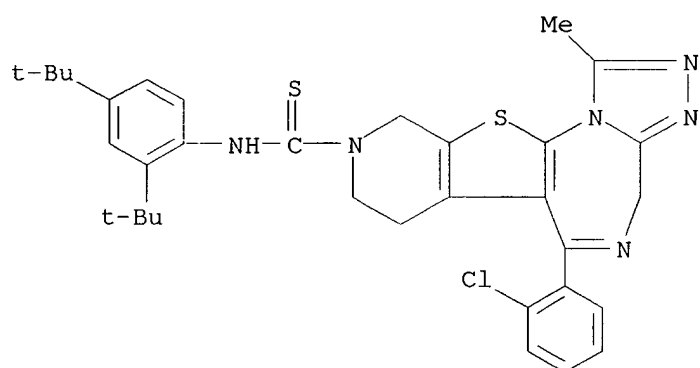
RN 132418-50-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

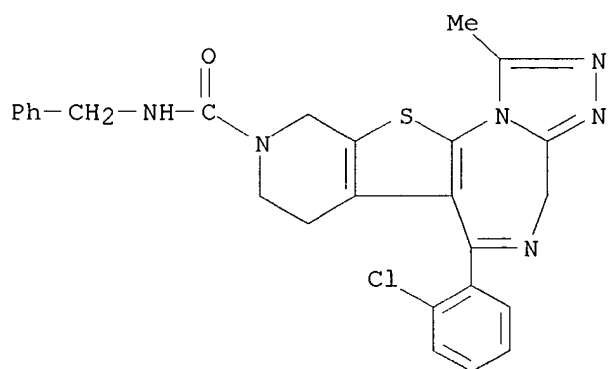
09/701,893



RN 132418-51-0 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, N-[2,4-bis(1,1-dimethylethyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



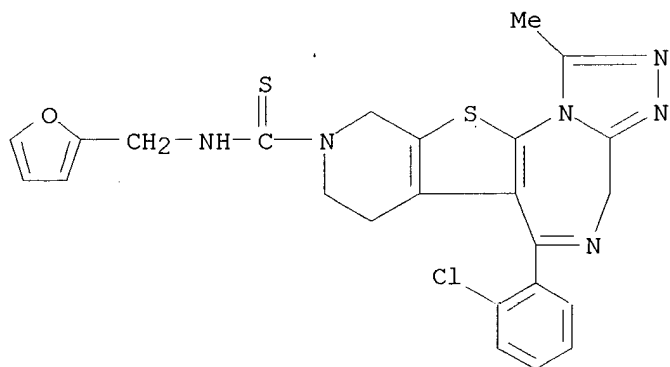
RN 132418-52-1 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



09/701,893

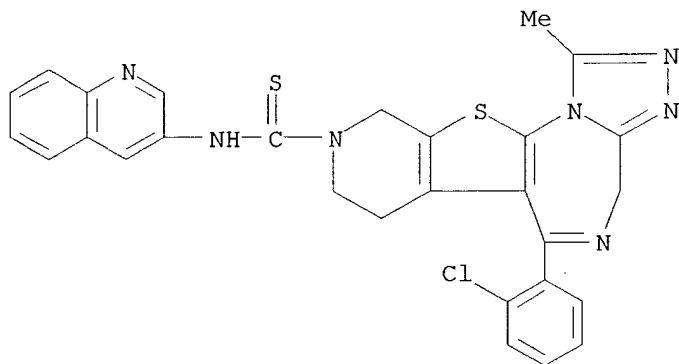
RN 132418-53-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylmethyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-54-3 CAPLUS

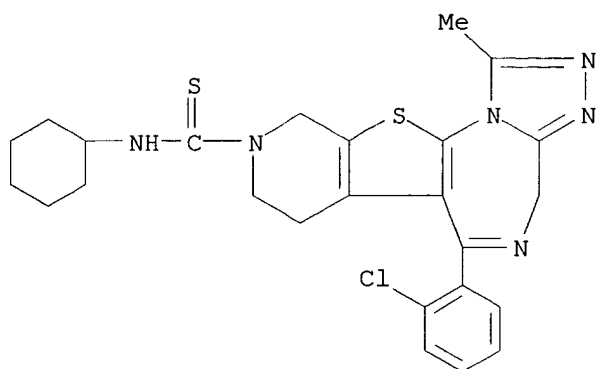
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-3-quinolinyl- (9CI) (CA INDEX NAME)



RN 132418-55-4 CAPLUS

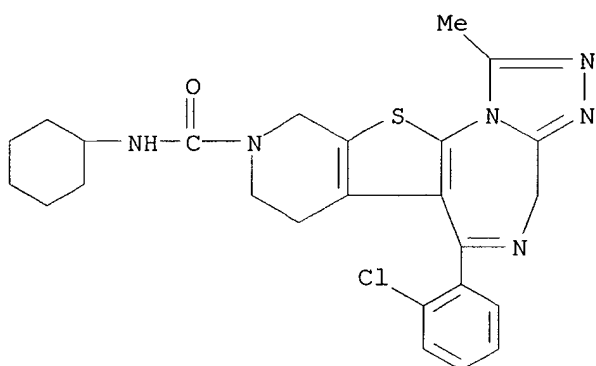
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



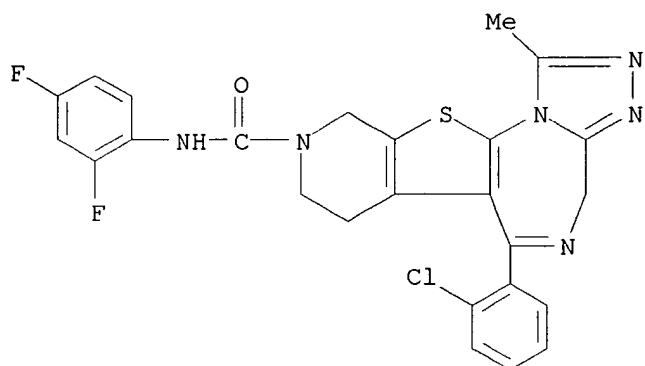
RN 132418-56-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-cyclohexyl-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(2,4-difluorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

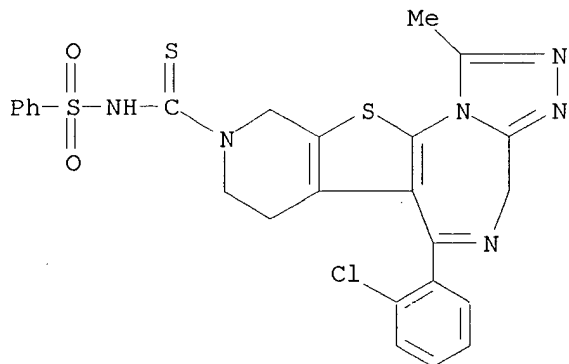


bi.

09/701,893

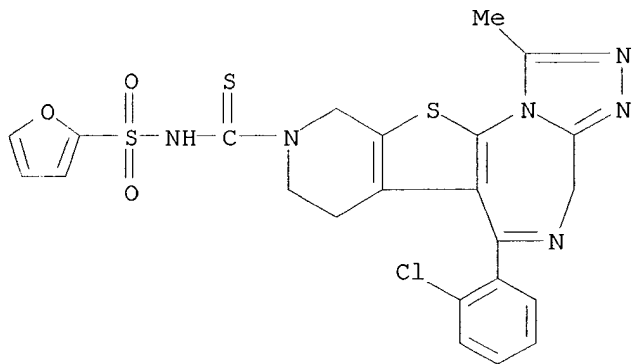
RN 132418-59-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 132418-60-1 CAPLUS

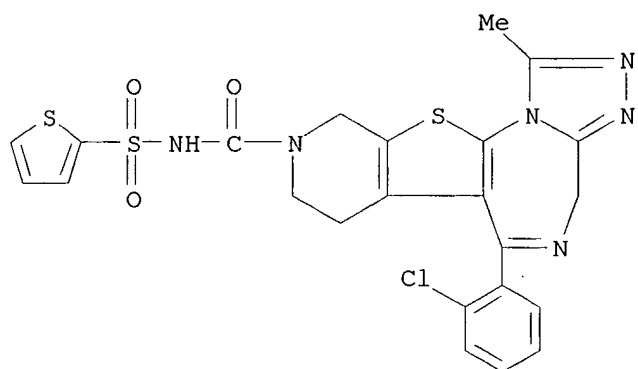
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-N-(2-furanylsulfonyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 132418-61-2 CAPLUS

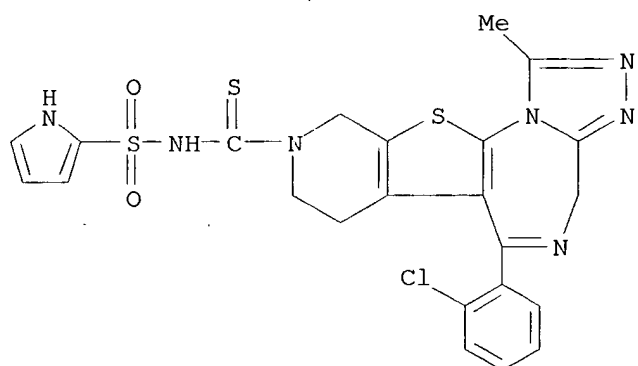
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

09/701,893



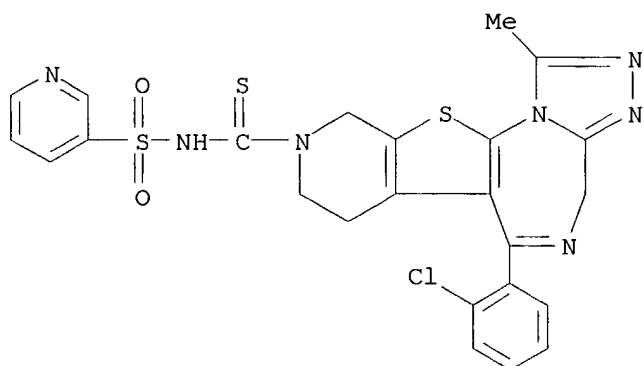
RN 132418-62-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(1H-pyrrol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)



RN 132418-63-4 CAPLUS

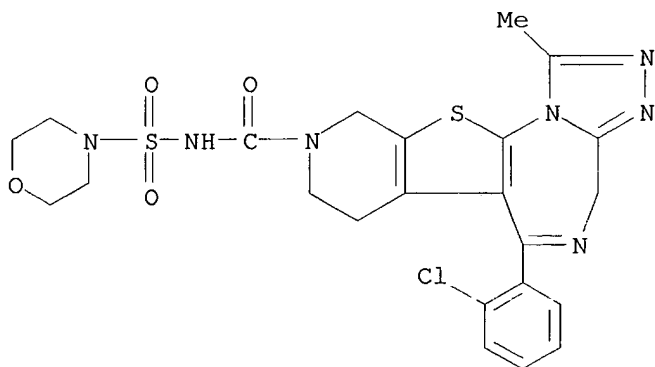
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(3-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



09/701,893

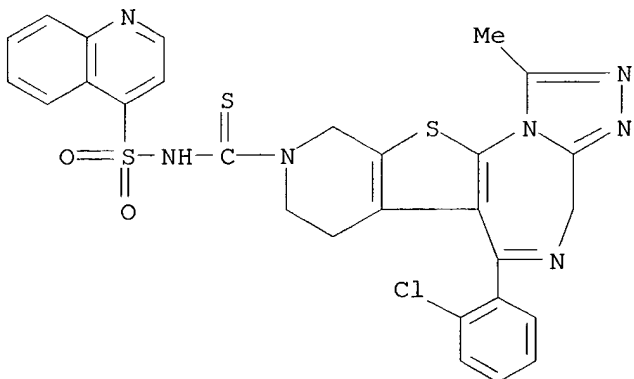
RN 132418-64-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-morpholinylsulfonyl)- (9CI) (CA INDEX NAME)



RN 132442-67-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-(4-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 88 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:122430 CAPLUS

DN 114:122430

TI Preparation of 9-sulfonyl-7,8,9,10-tetrahydro-4H-pyrido[4',3':4,5]thieno[3,2-f]-1,2,4-triazolo[4,3-a]-1,21-diazepines as platelet activating factor (PAF) antagonists

IN Esanu, Andre; Braquet, Pierre; Martin, Christiane; Laurent, Jean Pierre

PA Societe de Conseils de Recherches et d'Applications Scientifiques, Fr.

SO Ger. Offen., 11 pp.

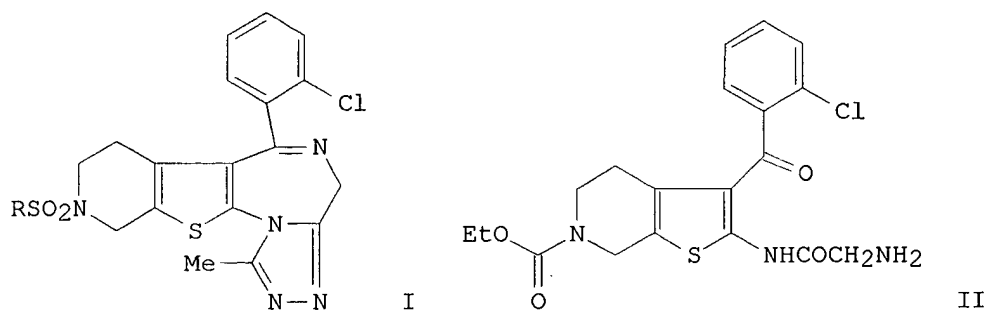
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4010361	A1	19901004	DE 1990-4010361	19900330
	NO 9001071	A	19901001	NO 1990-1071	19900307
	NO 173606	B	19930927		
	NO 173606	C	19940105		
	ZA 9001764	A	19901228	ZA 1990-1764	19900307
	AT 9000566	A	19911015	AT 1990-566	19900309
	AT 394560	B	19920511		
	SE 9000872	A	19901001	SE 1990-872	19900312
	SE 505420	C2	19970825		
	NL 9000625	A	19901016	NL 1990-625	19900319
	US 5049560	A	19910917	US 1990-496410	19900320
	BE 1003698	A3	19920526	BE 1990-342	19900327
	GB 2229724	A1	19901003	GB 1990-7075	19900329
	GB 2229724	B2	19920415		
	CH 680589	A	19920930	CH 1990-1046	19900329
	CA 2013519	AA	19900930	CA 1990-2013519	19900330
	DK 9000809	A	19901001	DK 1990-809	19900330
	AU 9052424	A1	19901004	AU 1990-52424	19900330
	AU 627408	B2	19920820		
	JP 02286684	A2	19901126	JP 1990-81416	19900330
	JP 06104667	B4	19941221		
	ES 2019244	A6	19910601	ES 1990-913	19900330
	FI 95037	B	19950831	FI 1990-1606	19900330
	FI 95037	C	19951211		
	FR 2645154	A1	19901005	FR 1990-4157	19900402
	FR 2645154	B1	19920417		
	FR 2645023	A1	19901005	FR 1990-4158	19900402
	FR 2645023	B1	19920417		
PRAI	GB 1989-7257		19890331		
OS	CASREACT 114:122430; MARPAT 114:122430				
GI					



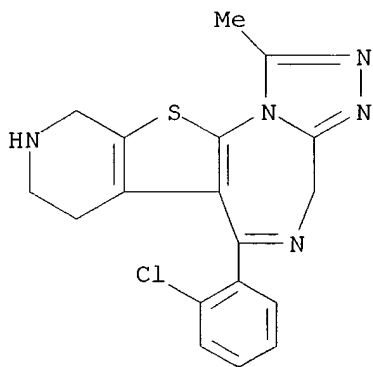
AB The title compds. [I; R = alkyl (substituted) Ph, furyl, thienyl, pyrrolyl, quinolinyl, naphthyl], were prepd. Thus, I [R = Me(CH₂)₁₅], prepd. in 11 steps from NCCH₂CO₂H and 2-ClC₆H₄COCl via pyridothiophene II, inhibited PAF-induced blood platelet aggregation in rabbits with an IC₅₀ of 9.63 .times. 10⁻⁸ nM. I at 10 mg/kg gave 7.8-52.1% protection against cerebral ischemia-induced brain damage in gerbils (based on Omega-3 site d.).

IT **114800-58-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for pyridothienotriazolodiazepine platelet activating factor antagonists)

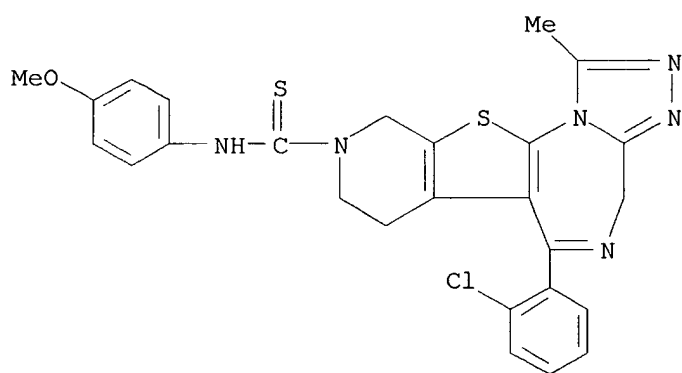
RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



L23 ANSWER 89 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1991:114867 CAPLUS
DN 114:114867
TI Influence of SK&F 95587 and BN 50730 on bronchoconstrictor responses in the cat
AU Dyson, M. C.; Bellan, J. A.; Minkes, R. K.; Beckerman, R. C.; Wegmann, M. J.; Braquet, P.; McNamara, D. B.; Kadowitz, P. J.
CS Sch. Med., Tulane Univ., New Orleans, LA, 70112, USA
SO J. Pharmacol. Exp. Ther. (1990), 255(3), 1320-7
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
AB The effects of SK&F 95587 [4[2-(benzenesulfonamido)ethyl]phenoxyacetic acid], a thromboxane (TX) receptor blocking agent, on bronchoconstrictor responses were investigated in paralyzed, anesthetized, mech. ventilated cats. I.v. injections of the TXA2 receptor mimics U-46619 [(15S)-hydroxy-11.alpha.,9.alpha.-(epoxymethano)prosta5Z, 13E-dienoic acid], and U-44069 (9,11-dideoxy-11.alpha.,9.alpha.-epoxymethano PGF2.alpha.) produced dose-related increases in transpulmonary pressure and lung resistance and decreases in dynamic compliance. After administration of SK&F 95587, 5 mg/kg i.v., bronchoconstrictor responses to U-46619 and U-44069 were reduced markedly, whereas airway responses to prostaglandin (PG)F2.alpha., were not altered. The duration of action of SK&F 95587 was greater than 3 h, and the blockade was overcome when 10-fold larger doses of the TXA2 mimics were administered. Bronchoconstrictor responses to platelet-activating factor (PAF) were blocked by SK&F 95587 and by the novel PAF receptor antagonist BN 50730 (I). I also blocked the fall in systemic arterial pressure in response to PAF. However, I did not influence airway responses to U-46619, PGF2.alpha., PGD2 or serotonin and had no effect on baseline bronchomotor tone or arterial pressure. The PAF receptor antagonism with I was overcome when 10-fold larger doses of PAF were administered and the dose-response curves for changes in lung resistance and dynamic compliance were shifted to the right in a parallel manner. The present data suggest that SK&F 95587 has selective TX receptor blocking activity, and that I has selective PAF receptor blocking properties in the airways of the cat. The present data also provide support for the hypothesis that bronchoconstrictor responses to PAF are mediated by specific receptors, which are coupled to a phospholipase and, when activated, result in the release of TXA2 and contraction of airway smooth muscle.
IT **132579-32-9**, BN 50730
RL: BIOL (Biological study)
(bronchoconstrictor response to platelet-activating factor blockade by, mechanism of)
RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



09/701,893

123 ANSWER 90 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1991:55582 CAPLUS

DN 114:55582

TI Pharmacological activities of a novel thienodiazepine derivative as a platelet-activating factor antagonist

AU Tsunoda, H.; Sakuma, Y.; Harada, K.; Muramoto, K.; Katayama, S.; Horie, T.; Shimomura, N.; Clark, R.; Miyazawa, S.; et al.

CS Tsukuba Res. Lab., Eisai Co., Ltd., Ibaraki, Japan

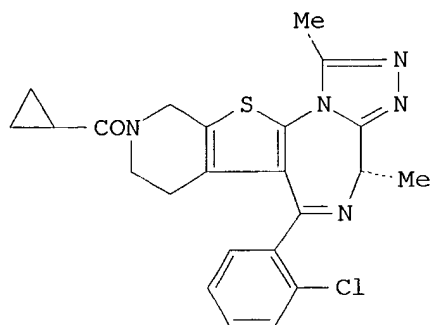
SO Arzneim.-Forsch. (1990), 40(11), 1201-5

CODEN: ARZNAD; ISSN: 0004-4172

DT Journal

LA English

GI



I

AB E-6123 (I) is a newly synthesized platelet-activating factor (PAF) antagonist. The effects of I on in vitro and in vivo PAF-induced responses were investigated. The IC₅₀ values of I on 3H-PAF binding to human and guinea pig platelets were 2.7 and 3.0 nmol/L, resp., and those on PAF-induced platelet aggregation in platelet-rich plasma of human, guinea pig and beagle dog were 10.1, 14.7 and 16 nmol/L, resp. Oral administration of I at 3 and 10 .mu.g/kg to dogs inhibited ex vivo PAF-induced platelet aggregation in a dose-dependent manner. In guinea pigs, I at 3 .mu.g/kg completely inhibited ex vivo PAF-induced platelet aggregation up to 8 h and the inhibition was still significant at 24 h after administration. Occupancy of the platelet PAF receptor by I at 3 and 24 h after administration amounted to 80% and 56%, resp. Bronchoconstriction induced by PAF injection in guinea pigs was inhibited dose-dependently by oral or i.v. administration of I at similar doses. The IC₅₀ value of I at 3 h after oral administration was 1 .mu.g/kg. Oral administration of I at 3 .mu.g/kg inhibited the bronchoconstriction by > 90% up to 8 h. Hematoconcn. induced by PAF injection in guinea pigs was inhibited by oral administration of I at 10 .mu.g/kg. I also protected mice from PAF injection-induced death in a dose-dependent manner. The in vitro and in vivo effects of I described above were compared with those of other PAF-antagonists. While the in vitro PAF-antagonistic activities of I were similar to those of two ref. antagonists, I showed the most potent in vivo inhibitory effects on the PAF-induced responses among the antagonists tested. In conclusion, I should prove valuable in pharmacol. and clin. research on the roles of PAF, and in therapy of diseases such as asthma, in which PAF is believed to play a pathol. role.

IT 131614-02-3, E 6123

RL: BIOL (Biological study)

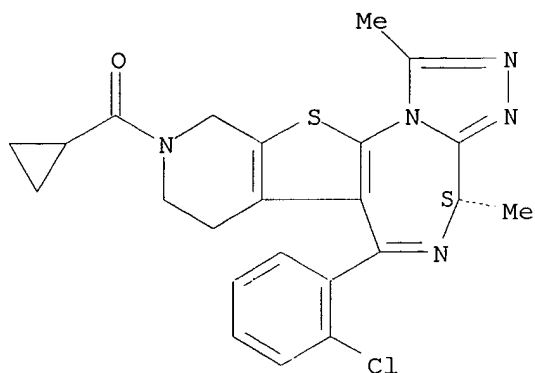
(as platelet-activating factor antagonist, pharmacol. of)

09/701,893

RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 91 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1990:612028 CAPLUS

DN 113:212028

TI Preparation of 8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepines as platelet activating factor (PAF) inhibitors

IN Okano, Kazuo; Miyazawa, Shuhei; Clark, Richard Stephen John; Abe, Shinya; Kawahara, Tetsuya; Shimomura, Naoyuki; Asano, Osamu; Yoshimura, Hiroyuki; Miyamoto, Mitsuaki; et al.

PA Eisai Co., Ltd., Japan

SO Eur. Pat. Appl., 135 pp.

CODEN: EPXXDW

DT Patent

LA English

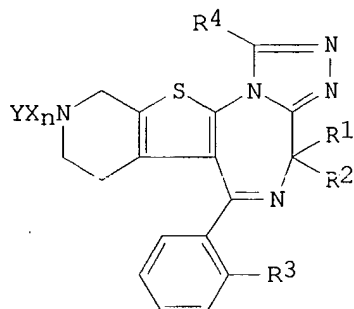
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	EP 367110	B1	19990811		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FI 95708	B	19951130	FI 1989-4867	19891013
	FI 95708	C	19960311		
	CA 2000985	AA	19900430	CA 1989-2000985	19891018
	AU 8943761	A1	19900503	AU 1989-43761	19891026
	AU 621413	B2	19920312		
	EP 606103	A1	19940713	EP 1994-101416	19891026
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	EP 677524	A1	19951018	EP 1995-111206	19891026
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 183187	E	19990815	AT 1989-119910	19891026
	NO 8904287	A	19900502	NO 1989-4287	19891027
	NO 175259	B	19940613		
	NO 175259	C	19940921		
	JP 02256682	A2	19901017	JP 1989-281300	19891027
	JP 2756004	B2	19980525		
	DK 8905406	A	19900501	DK 1989-5406	19891030
	CN 1042356	A	19900523	CN 1989-108238	19891030
	CN 1028640	B	19950531		
	HU 53106	A2	19900928	HU 1989-5609	19891030
	HU 217127	B	19991129		
	DD 293587	A5	19910905	DD 1989-334044	19891030
	RU 2117670	C1	19980820	RU 1989-4742387	19891030
	US 5382579	A	19950117	US 1991-751632	19910826
	US 5221671	A	19930622	US 1991-778563	19911017
	NO 9203459	A	19900502	NO 1992-3459	19920904
	US 5438045	A	19950801	US 1993-52721	19930427
	US 5304553	A	19940419	US 1993-68349	19930528
	CN 1121076	A	19960424	CN 1994-100504	19940117
	CN 1036520	B	19971126		
	US 5409909	A	19950425	US 1994-214850	19940318
	US 5482937	A	19960109	US 1994-318971	19941006
	US 5468740	A	19951121	US 1995-386533	19950210
PRAI	JP 1988-275460		19881031		
	JP 1988-297068		19881124		
	JP 1988-318016		19881216		
	JP 1988-331622		19881228		
	US 1989-421929		19891016		
	EP 1989-119910		19891026		
	NO 1989-4287		19891027		

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US 1990-506928	19900410
US 1991-751632	19910826
US 1991-778563	19911017
US 1993-52721	19930427
US 1994-318971	19941006

OS MARPAT 113:212028
GI



AB Title compds. I (R1, R2 = H, alkyl; R3 = H, halo; R4 = H, alkyl; X = O2C, R5NCO, R5 = H, alkyl, R6OP(O)O, R6 = alkyl, SO2; n = 0, 1; Y = (un)substituted cycloalkyl, cycloalkylalkyl, alkynyl, alkylnitrido, nitrilophenyl, heterocyclalkyl, arylalkyl, arylalkenyl, cyclopropylalkenyl, etc.) are prepd. as PAF inhibitors; I are useful in treatment of allergic and asthmatic diseases. 1-Cyano-1-methylethyl Ph carbonate and 6-(2-chlorophenyl)-11-methyl-2,3,4,5-tetrahydro-8H-pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine in CHCl3 were heated at 120.degree. for 1 h to give I (R1 = R2 = H; R3 = Cl; R4 = Me; YXn = NCCMe2O2C) (II). In a PAF receptor binding assay to human platelet the IC50 for II was 0.0033 .mu.M.

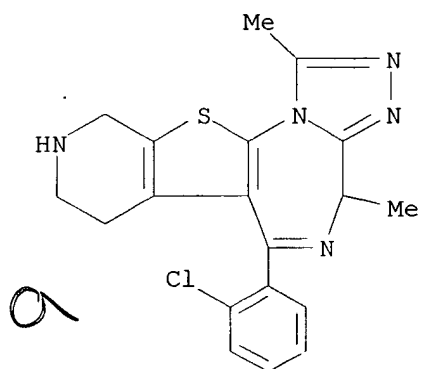
IT **130311-75-0P 130311-76-1P 130311-77-2P**
130311-97-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of platelet activating factor
inhibitors)

RN 130311-75-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl- (9CI) (CA INDEX
NAME)

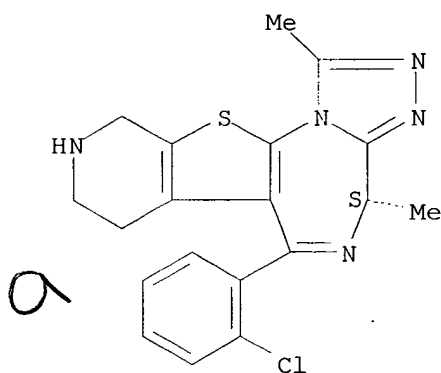
09/701,893



RN 130311-76-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (S)- (9CI) (CA
INDEX NAME)

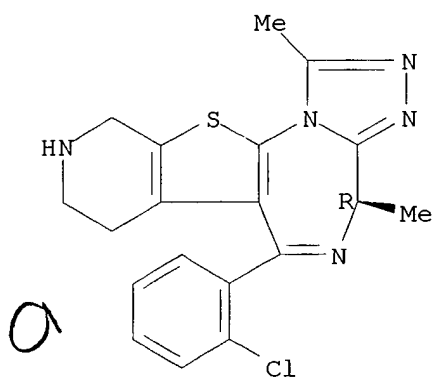
Absolute stereochemistry.



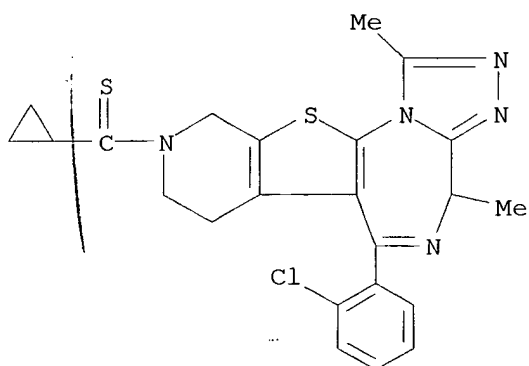
RN 130311-77-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



PM 130311-97-6 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-(cyclopropylthioxomethyl)-7,8,9,10-tetrahydro-1,4-
 dimethyl- (9CI) (CA INDEX NAME)



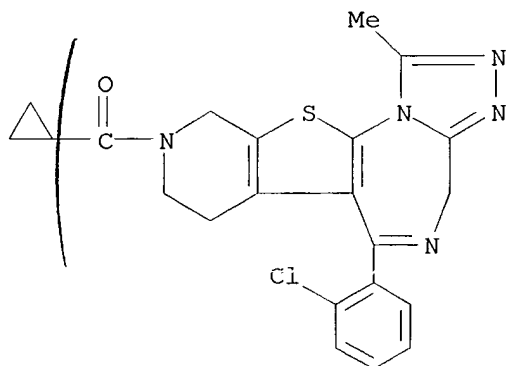
IT 130310-39-3P 130310-40-6P 130310-41-7P
 130310-42-8P 130310-50-8P 130310-52-0P
 130310-53-1P 130310-54-2P 130310-55-3P
 130310-56-4P 130310-57-5P 130310-63-3P
 130310-64-4P 130310-68-8P 130310-69-9P
 130310-70-2P 130310-71-3P 130310-72-4P
 130310-73-5P 130310-74-6P 130310-75-7P
 130310-76-8P 130310-77-9P 130310-78-0P
 130310-79-1P 130310-80-4P 130310-81-5P
 130310-82-6P 130310-85-9P 130310-87-1P
 130310-88-2P 130310-92-8P 130310-93-9P
 130310-97-3P 130310-98-4P 130310-99-5P
 130311-02-3P 130311-03-4P 130311-07-8P
 130311-09-0P 130311-10-3P 130311-11-4P
 130311-12-5P 130311-14-7P 130311-15-8P
 130311-16-9P 130311-17-0P 130311-18-1P
 130311-19-2P 130311-20-5P 130311-22-7P
 130311-24-9P 130311-25-0P 130311-26-1P
 130311-27-2P 130311-98-7P 130311-99-8P
 130335-42-1P 130335-43-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)

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(prepn. of, as platelet activating factor inhibitor)

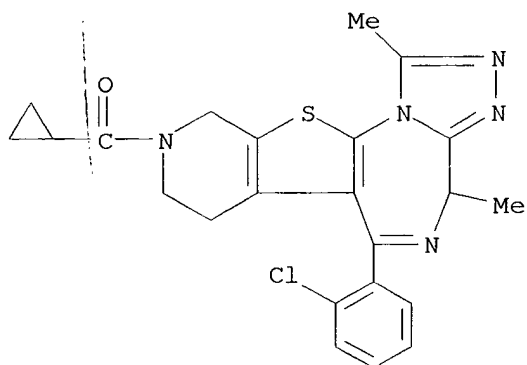
RN 130310-39-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



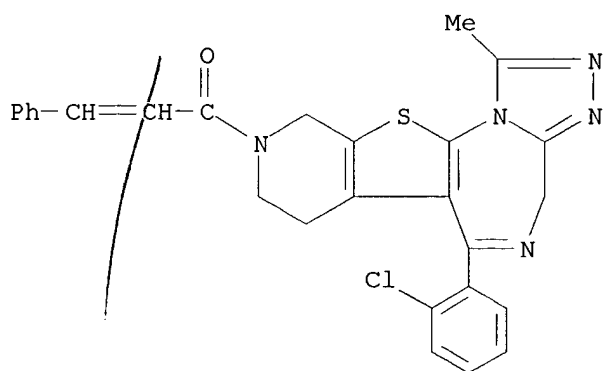
RN 130310-40-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl- (9CI) (CA INDEX NAME)



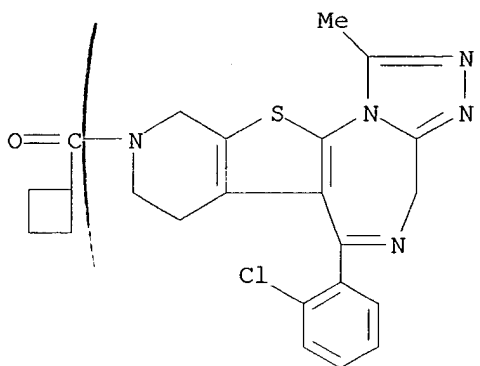
RN 130310-41-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(1-oxo-3-phenyl-2-
propenyl)- (9CI) (CA INDEX NAME)



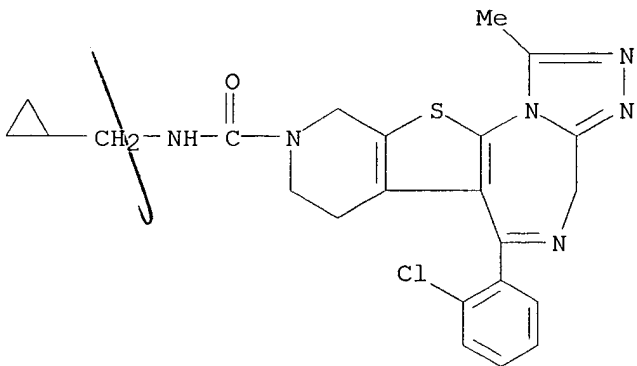
RN 130310-42-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclobutylcarbonyl)-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



RN 130310-50-8 CAPLUS

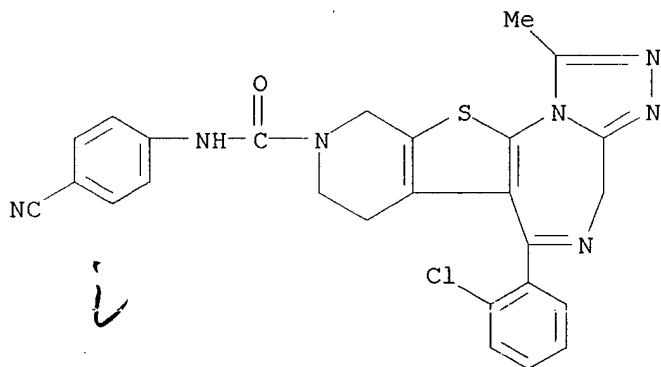
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(cyclopropylmethyl)-7,10-dihydro-1-
methyl- (9CI) (CA INDEX NAME)



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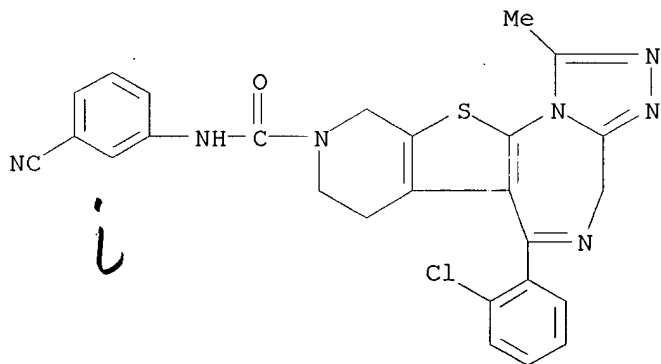
RN 130310-52-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(4-cyanophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



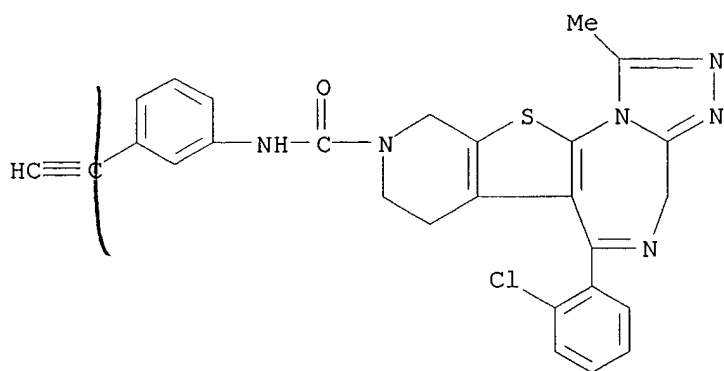
RN 130310-53-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(3-cyanophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



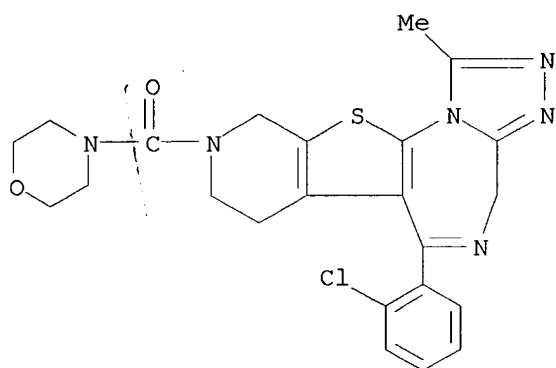
RN 130310-54-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(3-ethynylphenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



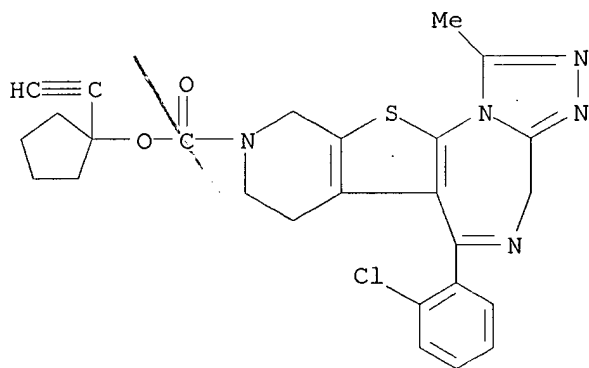
RN 130310-55-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(4-morpholinylcarbonyl)-
(9CI) (CA INDEX NAME)



RN 130310-56-4 CAPLUS

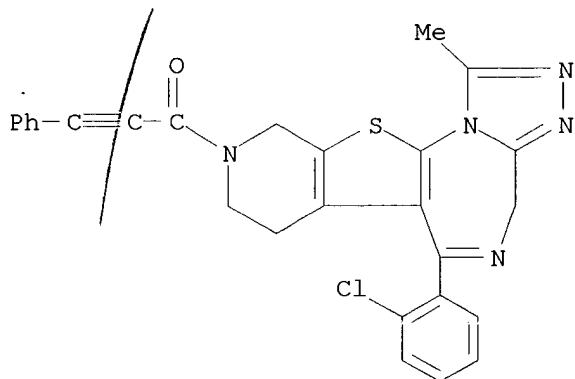
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-,
1-ethynylcyclopentyl ester (9CI) (CA INDEX NAME)



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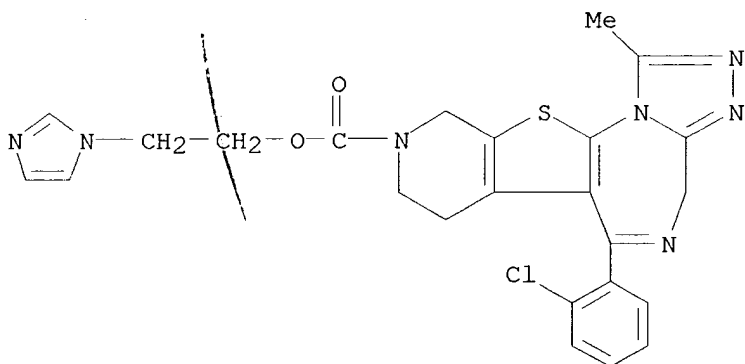
RN 130310-57-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(1-oxo-3-phenyl-2-
propynyl)- (9CI) (CA INDEX NAME)



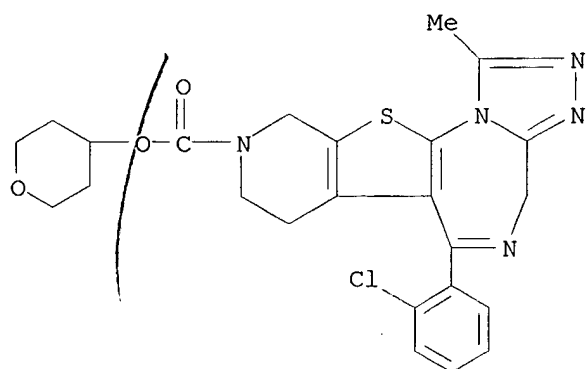
RN 130310-63-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-,
2-(1H-imidazol-1-yl)ethyl ester (9CI) (CA INDEX NAME)



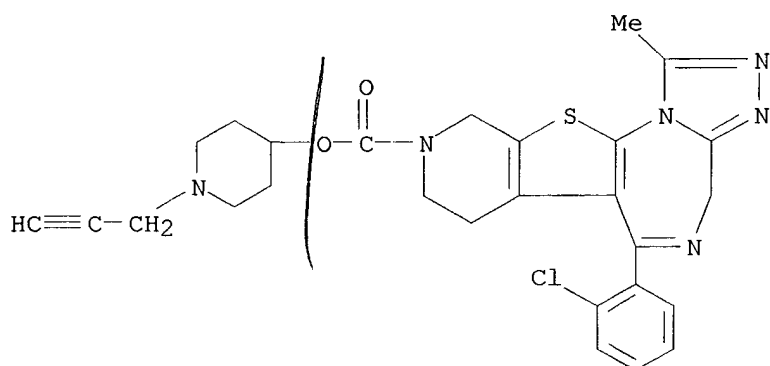
RN 130310-64-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-,
tetrahydro-2H-pyran-4-yl ester (9CI) (CA INDEX NAME)



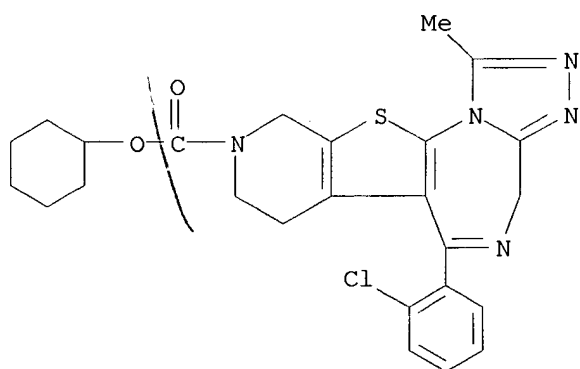
RN 130310-68-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 1-(2-propynyl)-4-piperidinyl ester (9CI) (CA INDEX NAME)



RN 130310-69-9 CAPLUS

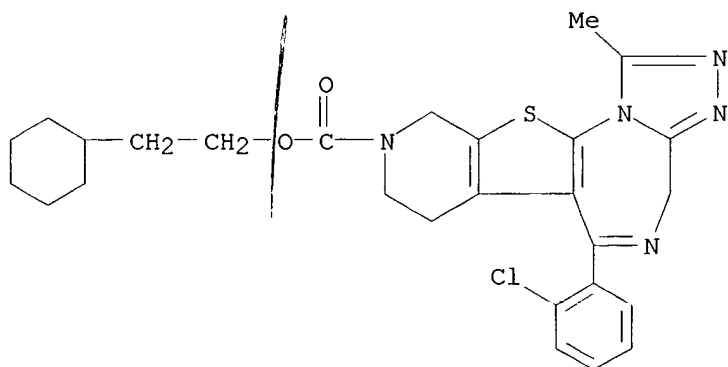
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)



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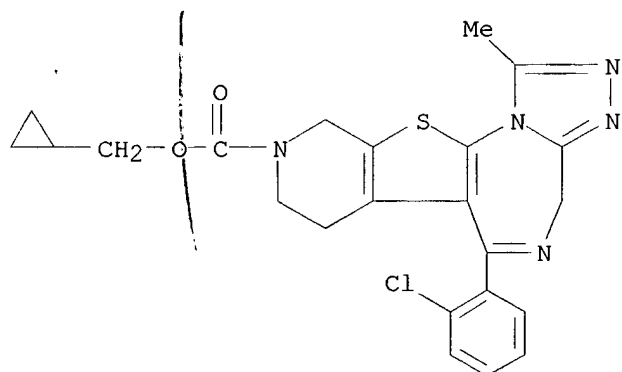
RN 130310-70-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-cyclohexylethyl ester (9CI) (CA INDEX NAME)



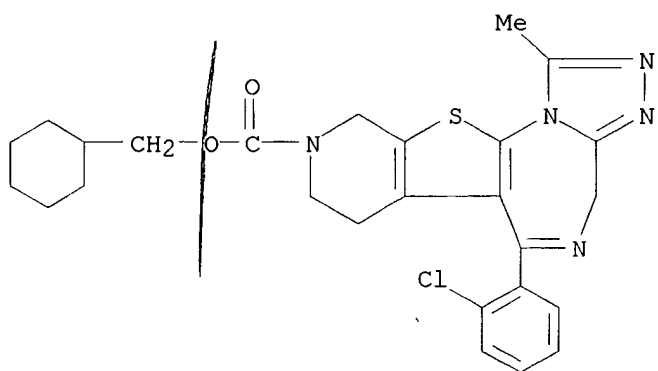
RN 130310-71-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)



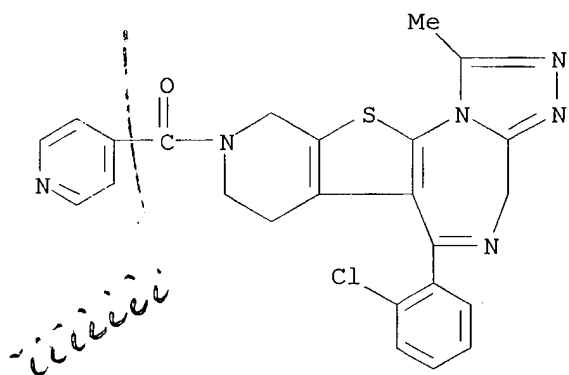
RN 130310-72-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, cyclohexylmethyl ester (9CI) (CA INDEX NAME)



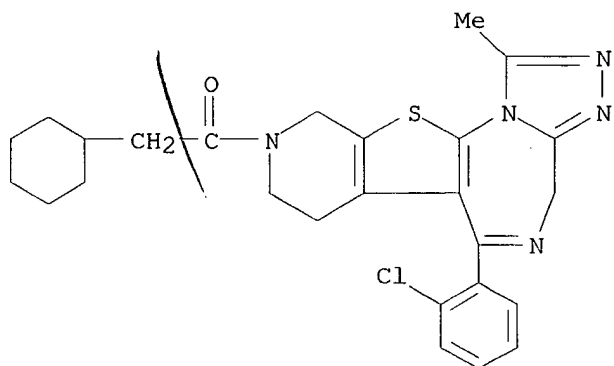
RN 130310-73-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(4-pyridinylcarbonyl)-
(9CI) (CA INDEX NAME)



RN 130310-74-6 CAPLUS

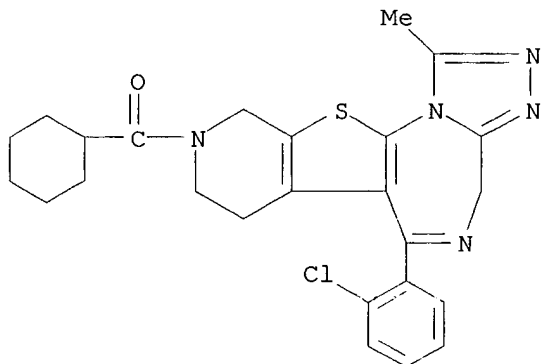
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclohexylacetyl)-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



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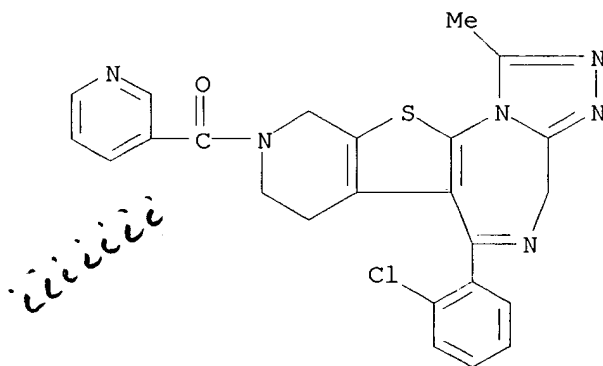
RN 130310-75-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclohexylcarbonyl)-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



RN 130310-76-8 CAPLUS

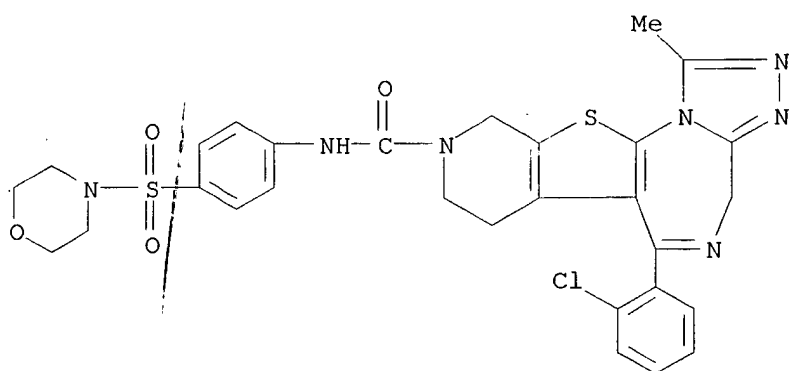
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(3-pyridinylcarbonyl)-
(9CI) (CA INDEX NAME)



RN 130310-77-9 CAPLUS

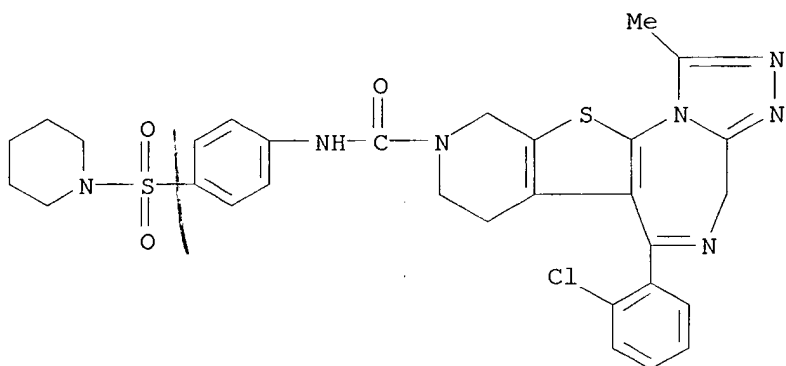
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(4-
morpholinylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

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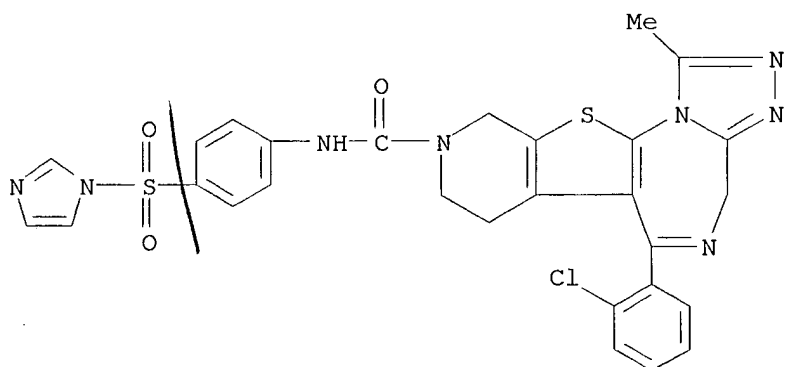
RN 130310-78-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-(1-piperidinylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 130310-79-1 CAPLUS

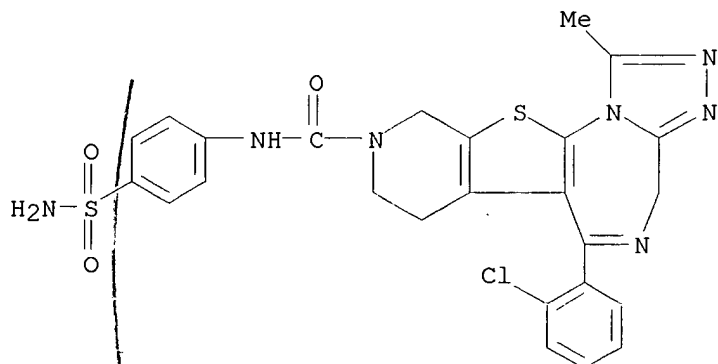
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-[4-(1H-imidazol-1-ylsulfonyl)phenyl]-1-methyl- (9CI) (CA INDEX NAME)



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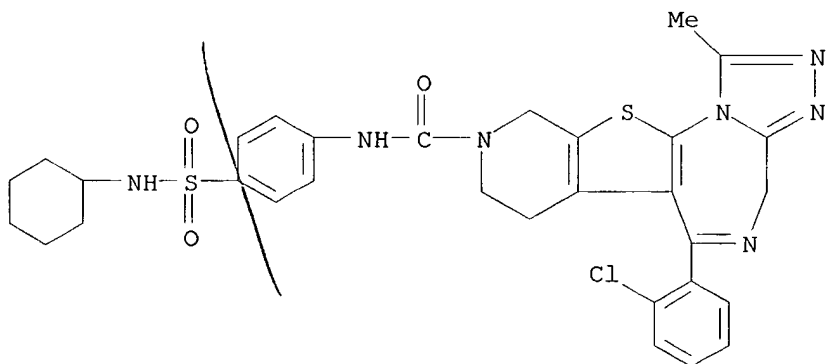
RN 130310-80-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, N-[4-(aminosulfonyl)phenyl]-6-(2-chlorophenyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



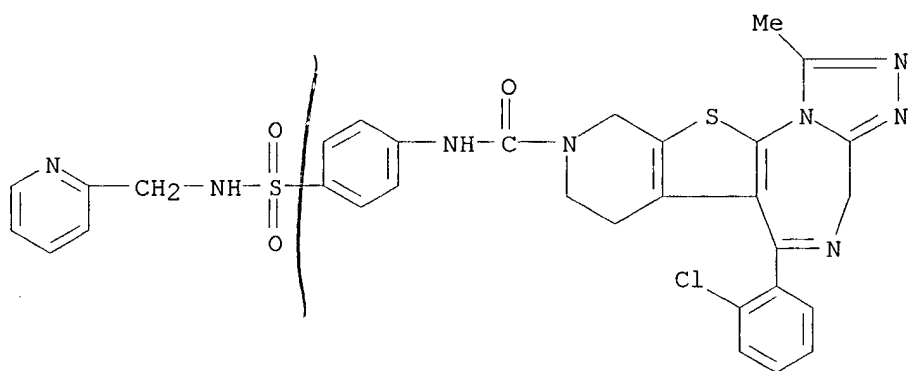
RN 130310-81-5 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-[(cyclohexylamino)sulfonyl]phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



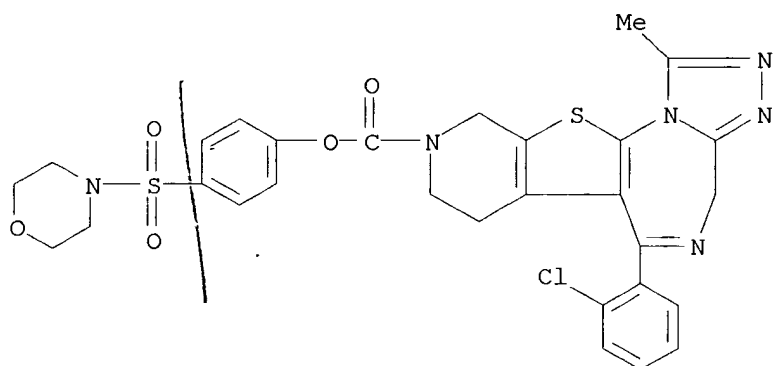
RN 130310-82-6 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[4-[[2-(pyridinylmethyl)amino]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



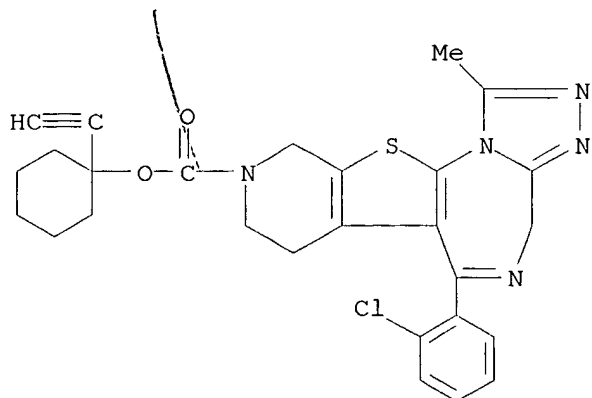
RN 130310-85-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 4-(4-morpholinylsulfonyl)phenyl ester (9CI) (CA INDEX NAME)



RN 130310-87-1 CAPLUS

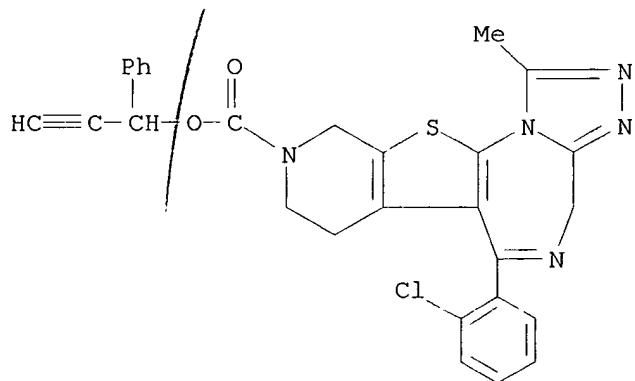
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 1-ethynylcyclohexyl ester (9CI) (CA INDEX NAME)



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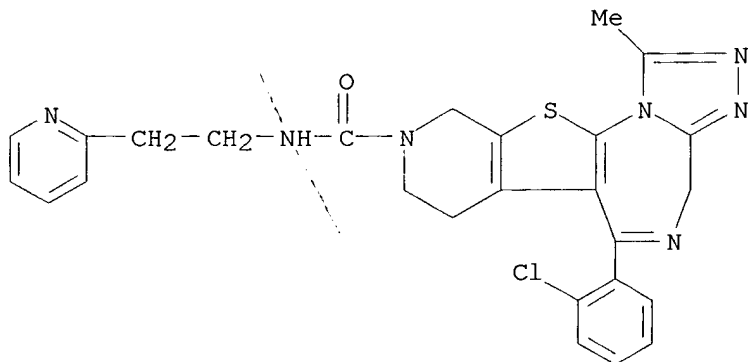
RN 130310-88-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 1-phenyl-2-propynyl ester (9CI) (CA INDEX NAME)



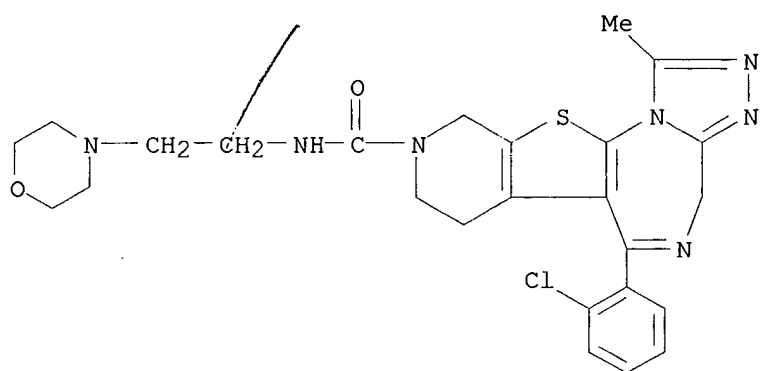
RN 130310-92-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



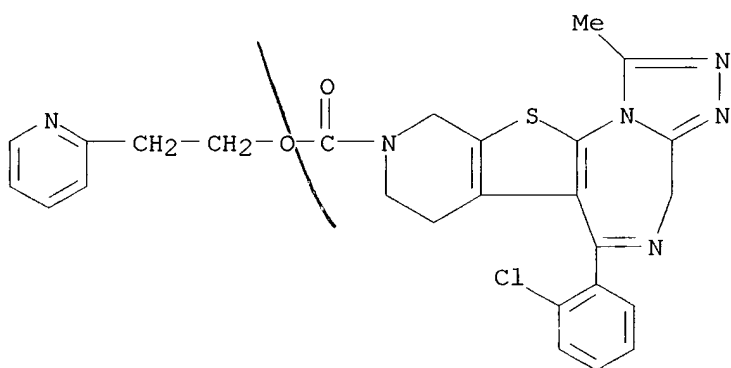
RN 130310-93-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



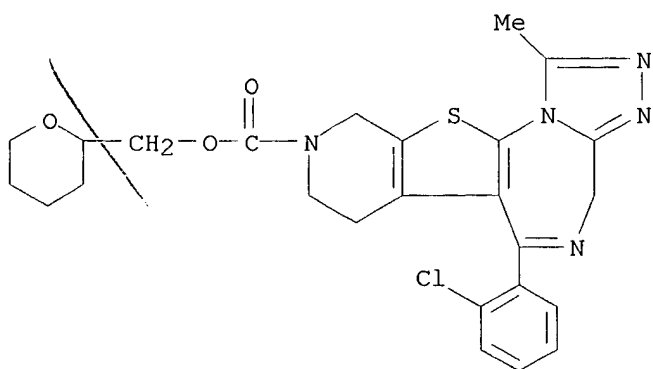
RN 130310-97-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-(2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)



RN 130310-98-4 CAPLUS

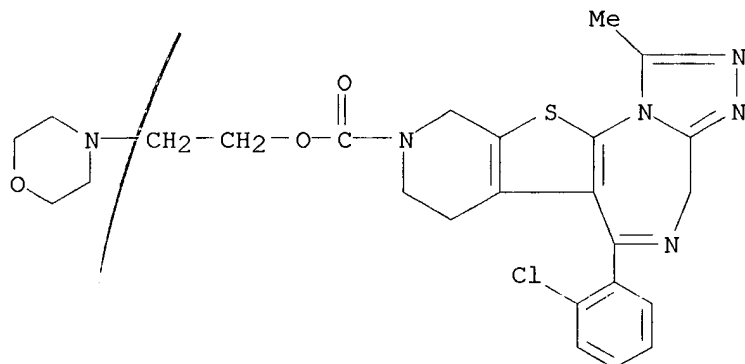
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, (tetrahydro-2H-pyran-2-yl)methyl ester (9CI) (CA INDEX NAME)



09/701,893

RN 130310-99-5 CAPLUS

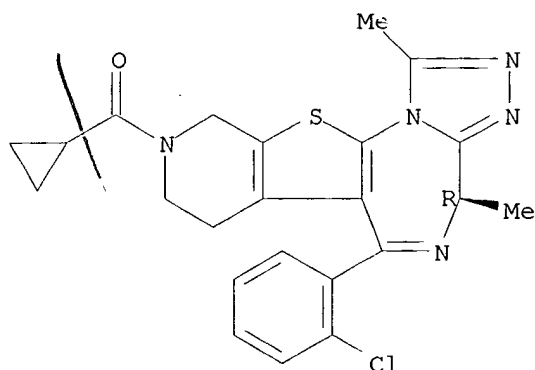
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-(4-morpholinyl)ethyl ester (9CI) (CA INDEX NAME)



RN 130311-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-, (R)- (9CI) (CA INDEX NAME)

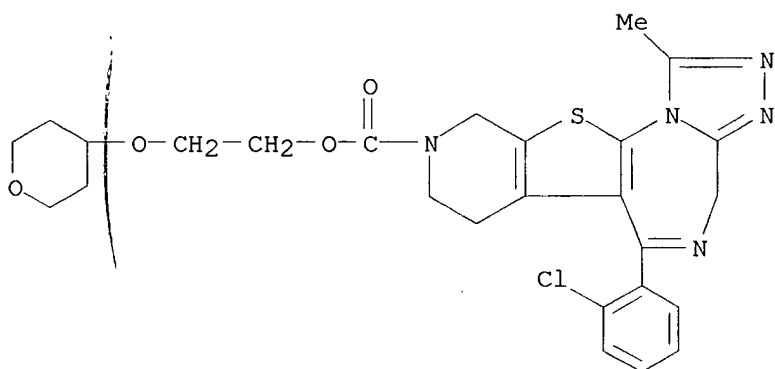
Absolute stereochemistry.



RN 130311-03-4 CAPLUS

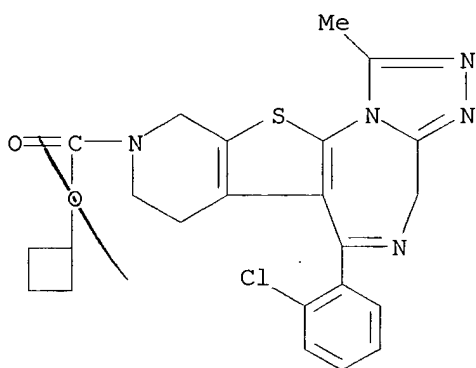
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-[(tetrahydro-2H-pyran-4-yl)oxy]ethyl ester (9CI) (CA INDEX NAME)

09/701,893



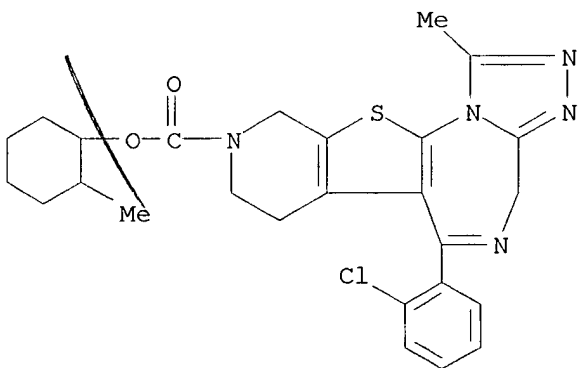
RN 130311-07-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, cyclobutyl ester (9CI) (CA INDEX NAME)



RN 130311-09-0 CAPLUS

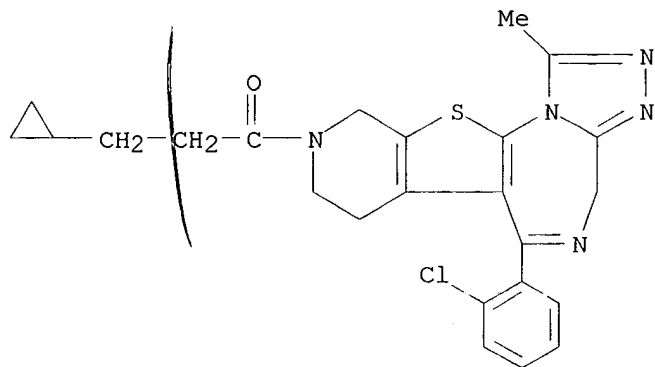
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-methylcyclohexyl ester (9CI) (CA INDEX NAME)



09/701,893

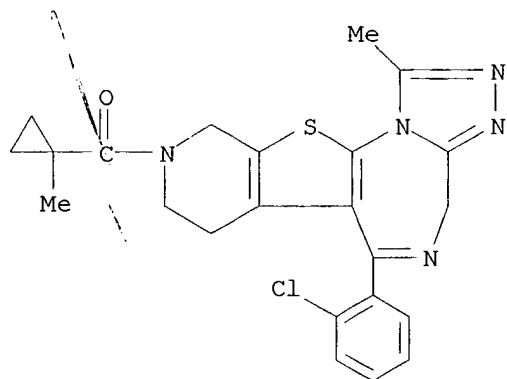
RN 130311-10-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(3-cyclopropyl-1-oxopropyl)-7,8,9,10-tetrahydro-1-
methyl- (9CI) (CA INDEX NAME)



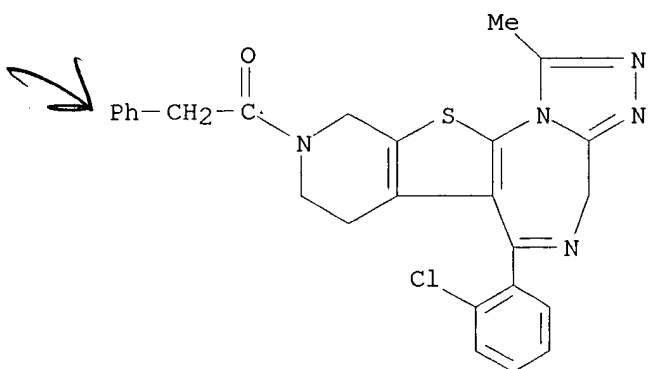
RN 130311-11-4 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(1-
methylcyclopropyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 130311-12-5 CAPLUS

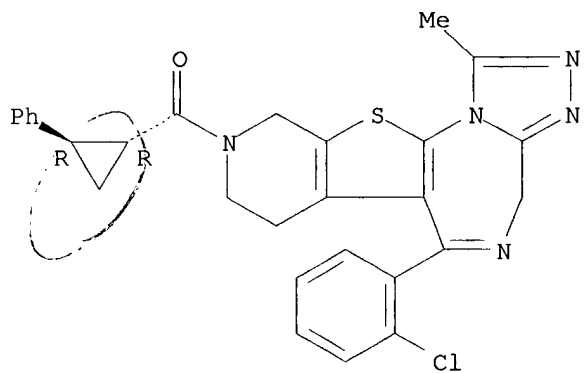
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(phenylacetyl)- (9CI)
(CA INDEX NAME)



RN 130311-14-7 CAPLUS

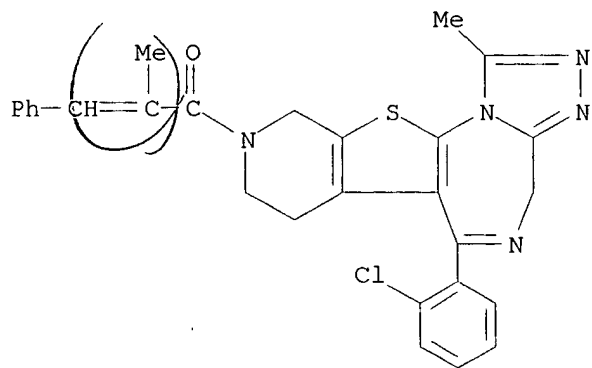
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(2-phenylcyclopropyl)carbonyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 130311-15-8 CAPLUS

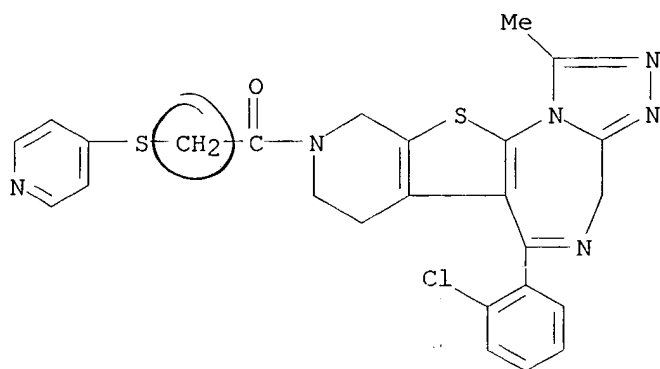
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(2-methyl-1-oxo-3-phenyl-2-propenyl)- (9CI) (CA INDEX NAME)



09/701,893

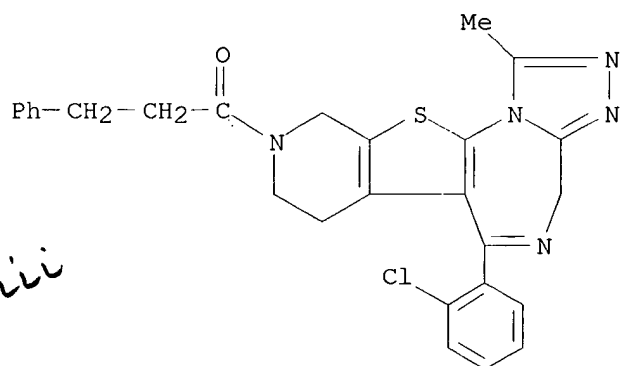
RN 130311-16-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(4-
pyridinylthio)acetyl]- (9CI) (CA INDEX NAME)



RN 130311-17-0 CAPLUS

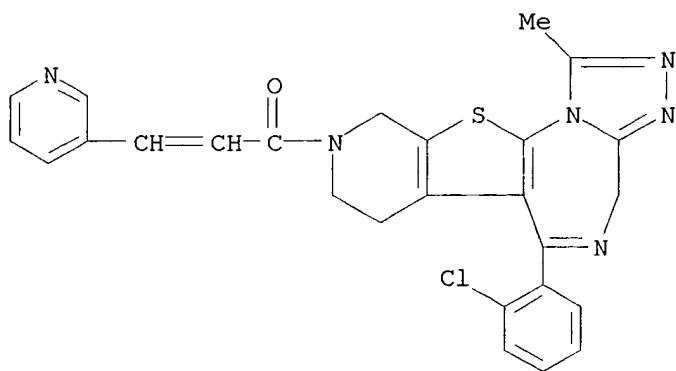
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(1-oxo-3-phenylpropyl)-
(9CI) (CA INDEX NAME)



RN 130311-18-1 CAPLUS

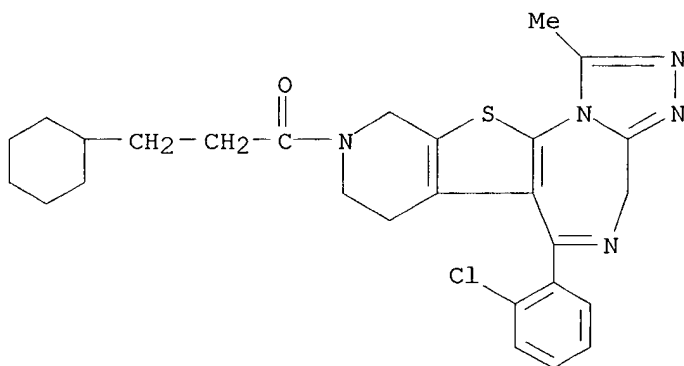
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-oxo-3-(3-pyridinyl)-2-
propenyl]- (9CI) (CA INDEX NAME)

09/701,893



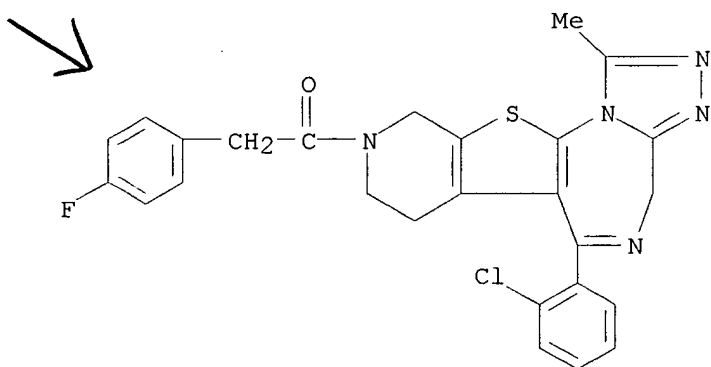
RN 130311-19-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(3-cyclohexyl-1-oxopropyl)-7,8,9,10-tetrahydro-1-
methyl- (9CI) (CA INDEX NAME)



RN 130311-20-5 CAPLUS

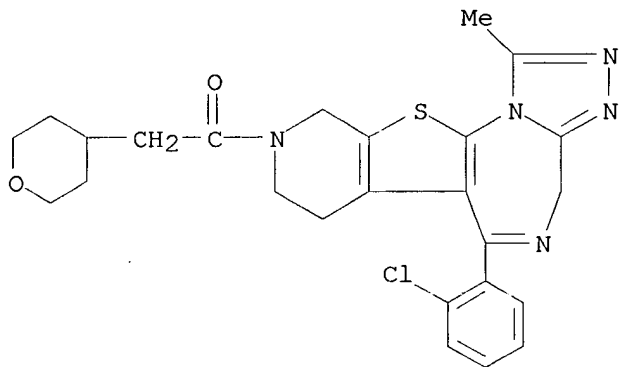
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-[(4-fluorophenyl)acetyl]-7,8,9,10-tetrahydro-1-methyl-
(9CI) (CA INDEX NAME)



09/701,893

RN 130311-22-7 CAPLUS

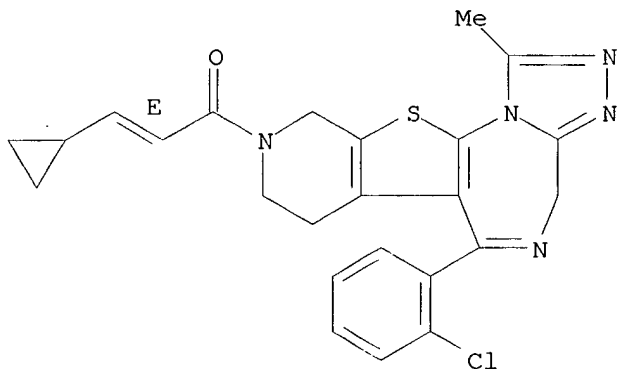
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[(tetrahydro-2H-pyran-4-yl)acetyl]- (9CI) (CA INDEX NAME)



RN 130311-24-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(3-cyclopropyl-1-oxo-2-propenyl)-7,8,9,10-tetrahydro-
1-methyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

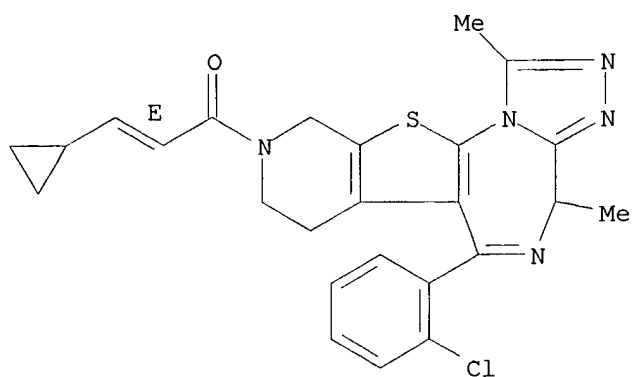


RN 130311-25-0 CAPLUS

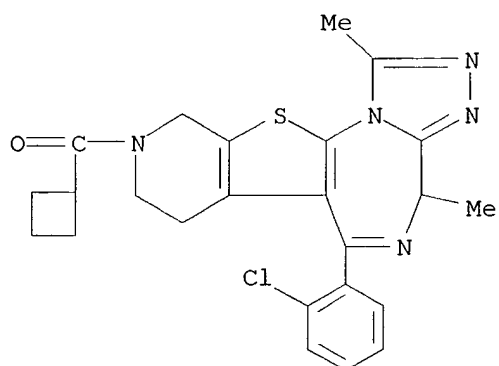
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(3-cyclopropyl-1-oxo-2-propenyl)-7,8,9,10-tetrahydro-
1,4-dimethyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

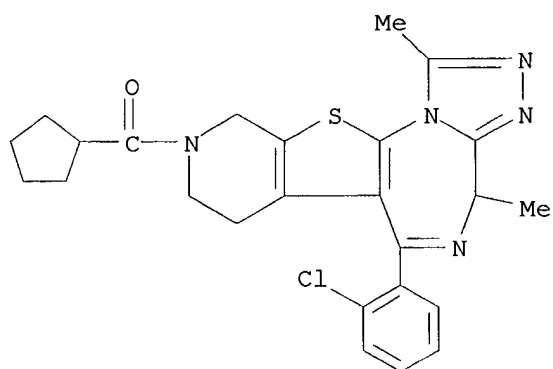
09/701,893



RN 130311-26-1 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclobutylcarbonyl)-7,8,9,10-tetrahydro-1,4-dimethyl-
(9CI) (CA INDEX NAME)



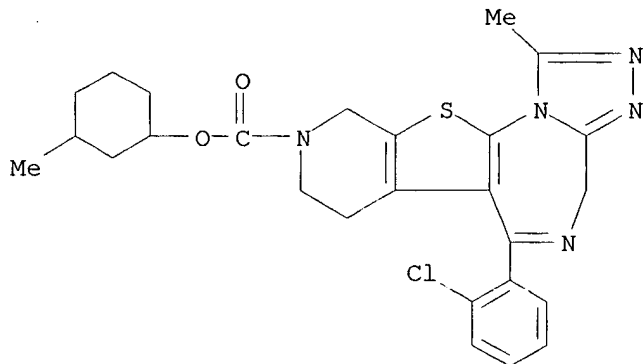
RN 130311-27-2 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopentylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl- (9CI) (CA INDEX NAME)



09/701,893

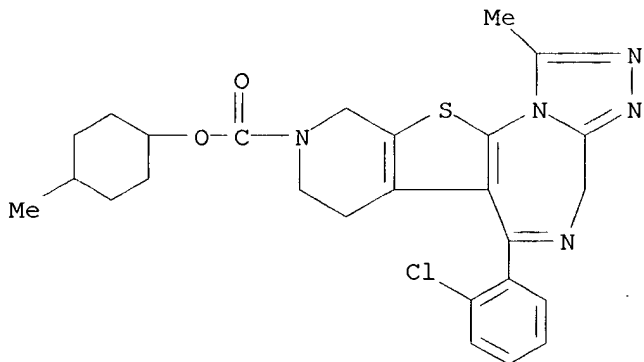
RN 130311-98-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 3-methylcyclohexyl ester (9CI) (CA INDEX NAME)



RN 130311-99-8 CAPLUS

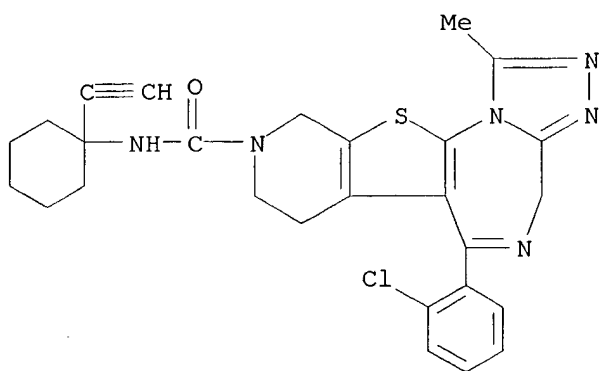
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 4-methylcyclohexyl ester (9CI) (CA INDEX NAME)



RN 130335-42-1 CAPLUS

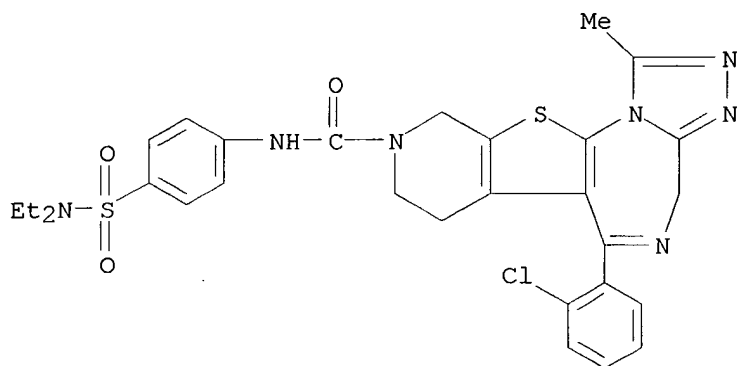
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(1-ethynylcyclohexyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 130335-43-2 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-[4-[(diethylamino)sulfonyl]phenyl]-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



IT 114800-58-7 130312-25-3

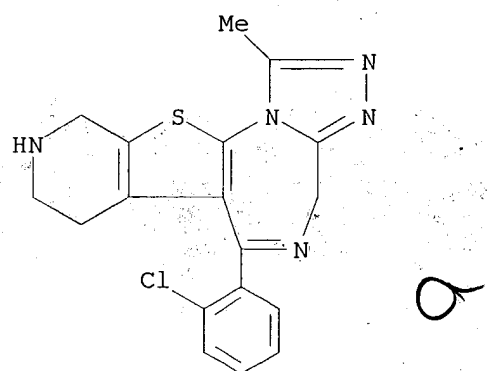
RL: RCT (Reactant)

(reaction of, in prepn. of platelet activating factor inhibitors)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 130312-25-3 CAPLUS

L23 ANSWER 92 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1988:529067 CAPLUS

DN 109:129067

TI Preparation of tetracyclic, fused-ring 1,4-diazepines as
platelet-activating factor (PAF) antagonistsIN Weber, Karl Heinz; Harreus, Albrecht; Stransky, Werner; Walther, Gerhard;
Casals, Stenzel Jorge; Muacevic, Gojko; Heuer, Hubert; Bechtel, Wolf
Dietrich

PA Boehringer Ingelheim K.-G., Fed. Rep. Ger.

SO Ger. Offen., 68 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3724031	A1	19880128	DE 1987-3724031	19870721
	EP 254245	A1	19880127	EP 1987-110443	19870718
	EP 254245	B1	19940928		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ES 2061452	T3	19941216	ES 1987-110443	19870718
	FI 8703180	A	19880123	FI 1987-3180	19870720
	PL 153970	B1	19910628	PL 1987-266884	19870720
	PL 157209	B1	19920529	PL 1987-287349	19870720
	DK 8703797	A	19880123	DK 1987-3797	19870721
	NO 8703041	A	19880125	NO 1987-3041	19870721
	NO 166942	B	19910610		
	NO 166942	C	19910918		
	JP 63033382	A2	19880213	JP 1987-182123	19870721
	JP 08005895	B4	19960124		
	ZA 8705333	A	19890329	ZA 1987-5333	19870721
	HU 50830	A2	19900328	HU 1987-3355	19870721
	HU 203354	B	19910729		
	DD 281389	A5	19900808	DD 1987-305190	19870721
	CS 274456	B2	19910411	CS 1987-5508	19870721
	CS 277445	B6	19930317	CS 1989-1930	19870721
	CS 277446	B6	19930317	CS 1989-1931	19870721
	AU 8776015	A1	19880128	AU 1987-76015	19870722
	AU 609408	B2	19910502		
	CA 1338287	A1	19960430	CA 1987-542748	19870722
	CZ 284052	B6	19980812	CZ 1989-2206	19890410
	SU 1738089	A3	19920530	SU 1989-4614791	19890817
	US 5532233	A	19960702	US 1994-302578	19940908
PRAI	DE 1986-3624647		19860722		
	US 1987-76515		19870722		
	US 1987-88758		19870824		
	US 1989-352527		19890516		
	US 1990-538582		19900614		
	US 1991-724654		19910702		
	US 1992-942556		19920909		
	US 1993-61392		19930513		
OS	CASREACT 109:129067; MARPAT 109:129067				
GI	For diagram(s), see printed CA Issue.				
AB	The title compds. [I; R1 = H, cycloalkyl, halo, (un)substituted alkyl, alkoxy; R2 = H, halo, cyano, CHO, OH, etherified or esterified OH, alkylthio, (un)modified CO ₂ H, amino, benzimidazolyl, (un)substituted 5-, 6-, or 7-membered heterocyclyl; R3 = pyridyl, (un)substituted Ph; R4 = H, alkyl, alkanoyl; R5 = H; R4R5 = bond; X, Y = R6C, N; R6 = R1,				

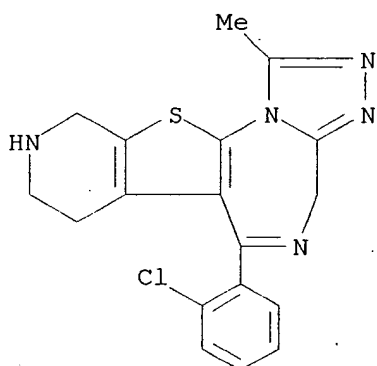
alkoxycarbonyl; Z = bond, Cl-6 alkylene; A = fused, unsatd., (un)substituted 5-, 6-, or 7-membered ring] and their stereoisomers and physiol. acceptable salts were prepd. as PAF antagonists. Cyclopentathienotriazolodiazepinecarboxylate II (R7 = EtO) was prepd. in 7 steps, starting with cyclocondensation of Et 3-oxocyclopentanecarboxylate with 2-ClC6H4COCH2CN. The ester was sapond. to give II (R7 = OH) which was treated with morpholine and 1,1'-carbonyldiimidazole to give morpholide II (R7 = morpholine) (III). III inhibited blood platelet aggregation with an IC50 of 0.3 .mu.M and, in the benzodiazepine receptor binding test, had an IC50 of 3600 .times. 10-9 M. In the same tests triazolam had an IC50 of 9 .mu.M and 1.4 .times. 10-9 M, resp. III is thus expected to have little CNS activity.

IT **114800-58-7P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as platelet-activating factor antagonist)

RN 114800-58-7 CAPLUS

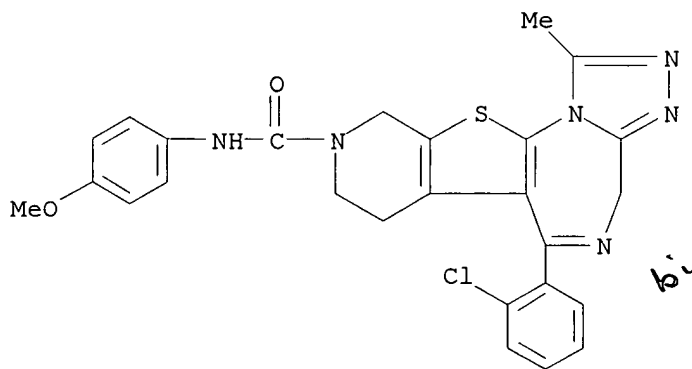
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



ref #4 of Aug 8, 2002

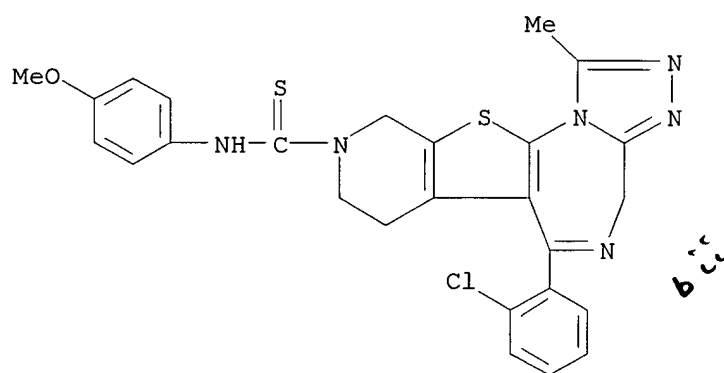
09/701,893

L23 ANSWER 44 OF 92 CAPLUS COPYRIGHT 2001 ACS
AN 1994:594811 CAPLUS
DN 121:194811
TI Simultaneous quantitative measurement of a new platelet activating factor antagonist (BN 50730) and its two main metabolites in human plasma and urine by LC-MS
AU Girault, J.; Longueville, D.; Malgouyat, J. M.; Istin, B.; Lecomte, G.; Fourtillan, J. B.
CS CEMAF Research Centre, Poitiers, 86000, Fr.
SO Chromatographia (1994), 39(3-4), 228-38
CODEN: CHRGB7; ISSN: 0009-5893
DT Journal
LA English
AB A simple and sensitive assay has been developed for the quant. measurement of a new platelet activating factor antagonist (BN 50730), and its two main metabolites (BN 50727 and BN 50922), at the picomole level in human plasma and urine. The three compds. of interest and the internal std. (BN 50765) were measured by combined LC-neg. chem. ionization MS. A simple solid-liq. extn. procedure was used to isolate the parent drug and the two metabolites. The MS was tuned to monitor the intense ion m/z 333 generated in the ion source by a dissociative capture process. The assay was on 1 mL plasma or 0.1 mL urine and the quantitation limit was calcd. as 1 ng.cntdot.mL-1. The very low relative std. deviations and mean percentages of error calcd. for within-day or between-day repeatability assays demonstrate the ruggedness of the technique for routine detn. in biol. fluids. Some preliminary results on the pharmacokinetics of the parent drug and its two main metabolites illustrate the applicability of this method.
IT 132418-35-0, BN 50727 132579-32-9, BN 50730
153339-88-9, BN 50922
RL: ANT (Analyte); ANST (Analytical study)
(LC-MS detn. of BN 50730 and metabolites in human plasma and urine)
RN 132418-35-0 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

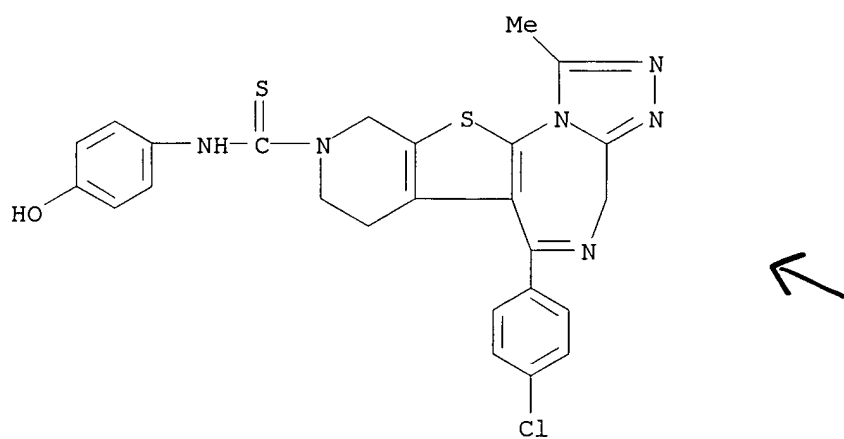


RN 132579-32-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 153339-88-9 CAPLUS
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(4-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)



L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

AN 1994:182706 CAPLUS

DN 120:182706

TI Prevention of chloroquine-induced electroretinographic damage by a new platelet-activating factor antagonist, BN 50730

AU Doly, Michel; Cluzel, Jacques; Millerin, Martine; Bonhomme, Brigitte; Braquet, Pierre

CS Lab. Biophys., Fac. Med., Clermont-Ferrand, F-63001, Fr.

SO Ophthalmic Res. (1993), 25(5), 314-18

CODEN: OPRSAQ; ISSN: 0030-3747

DT Journal

LA English

AB Chloroquine retinopathy is a severe toxic retinal impairment which may result in loss of vision by alterations of the retinal pigment epithelium and photoreceptors. Currently, there is no specific treatment for this retinopathy. Platelet-activating factor (PAF) is known to modulate retinal function and is one of the major immunomediators of the retina. In order to test the possible involvement of PAF in chloroquine-induced retinopathy and the effectiveness of PAF antagonists in the prevention of this condition, the authors investigated the effects of BN 50730, a specific PAF antagonist, on the electroretinogram (ERG) of the isolated rat retina exposed to chloroquine. When retinas from normal rats were perfused with chloroquine (10⁻⁶ M), a marked and rapid decrease in b-wave amplitude was obsd. In contrast, chloroquine had no effect on the b-wave of the retina isolated from animals pretreated with the PAF antagonist BN 50730 (30 mg/kg/day, i.p., for 5 days). The results obtained indicate that (i) chloroquine is a toxic drug for retinal function, (ii) PAF plays a key role in the mediation of chloroquine retinopathy and (iii) PAF antagonists may constitute valuable agents for the treatment of this retinal impairment.

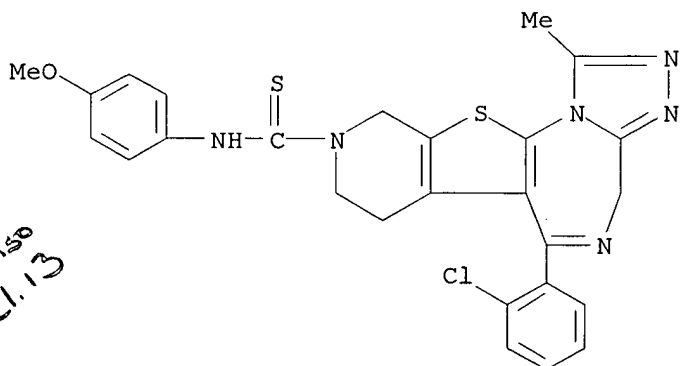
IT 132579-32-9, BN 50730

RL: BIOL (Biological study)

(chloroquine-induced retinopathy prevention by, as platelet-activating factor antagonist)

RN 132579-32-9 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carbothioamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

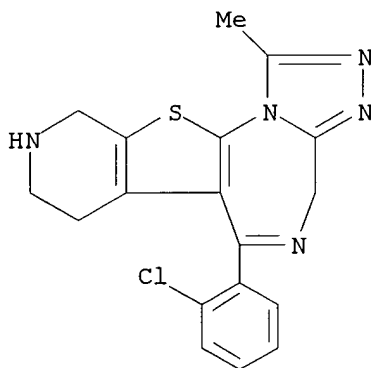


IT 65154-06-5, Blood-platelet activating factor

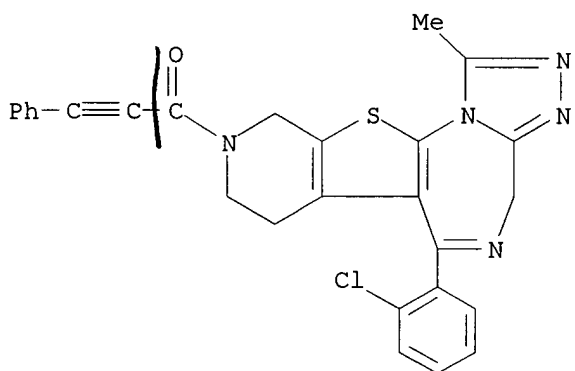
RL: PROC (Process)

(in chloroquine-induced retinopathy, BN 50730 prevention of)

7/99/92
 L23 ANSWER 71 OF 92 CAPLUS COPYRIGHT 2001 ACS
 AN 1992:174118 CAPLUS
 DN 116:174118
 TI Structure-activity studies on triazolothienodiazepine derivatives as platelet-activating factor antagonists
 AU Miyazawa, Shuhei; Okano, Kazuo; Shimomura, Naoyuki; Clark, Richard S. J.; Kawahara, Tetsuya; Asano, Osamu; Yoshimura, Hiroyuki; Miyamoto, Mituaki; Sakuma, Yoshinori; et al.
 CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan
 SO Chem. Pharm. Bull. (1991), 39(12), 3215-20
 CODEN: CPBTAL; ISSN: 0009-2363
 DT Journal
 LA English
 GI For diagram(s), see printed CA Issue.
 AB Title compds. I (R = HC.tplbond.CCH2, NCCMe2O2C, 4-FC6H4CH2CO, etc., R1 = R2 = H; R = HC.tplbond.CCH2CH2O2C, R1,R2 = H, Me, Et; R = NCCMe2O2C, cyclopropanecarbonyl, R1 = Me, R2 = H) were prepd. and their structure-activity relationship as platelet-activating factor antagonists was examd. Thus, I (R = R1 = R2 = H) reacted with HC.tplbond.CCH2Br to give I (R = HC.tplbond.CCH2). Introducing a Me group into the 8-position of the thienodiazepine nucleus leads to a longer duration of action.
 IT **114800-58-7**
 RL: RCT (Reactant)
 (alkylation and acylation of)
 RN 114800-58-7 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

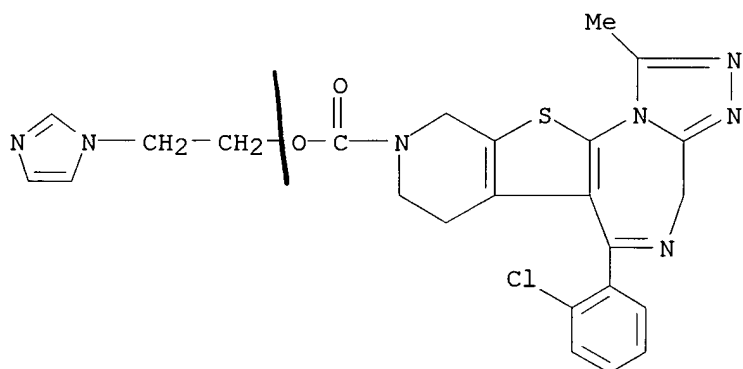


IT **130310-57-5 130310-63-3 140167-26-6**
140167-27-7 140167-28-8
 RL: RCT (Reactant)
 (platelet-activating factor antagonistic activity of)
 RN 130310-57-5 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-(1-oxo-3-phenyl-2-propynyl)- (9CI) (CA INDEX NAME)



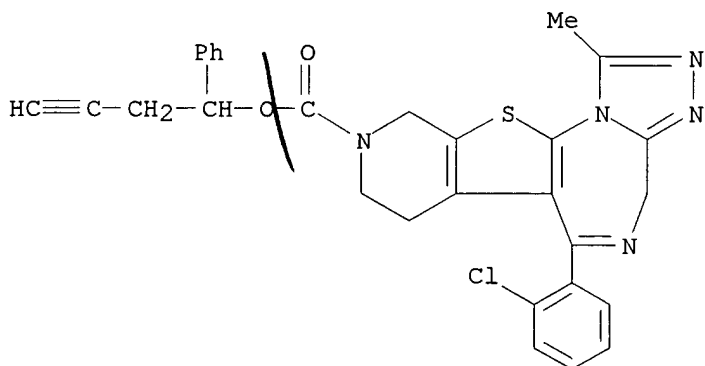
RN 130310-63-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 2-(1H-imidazol-1-yl)ethyl ester (9CI) (CA INDEX NAME)



RN 140167-26-6 CAPLUS

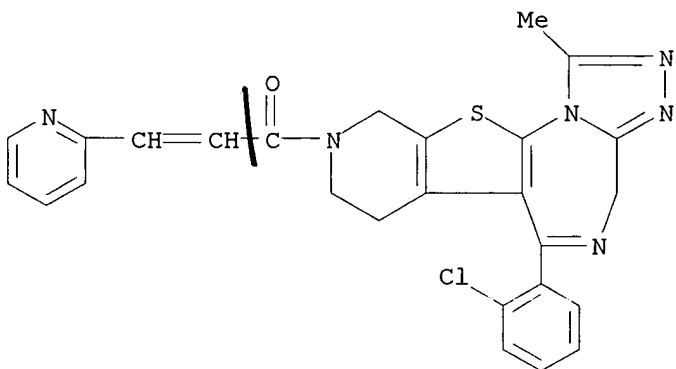
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxylic acid, 6-(2-chlorophenyl)-7,10-dihydro-1-methyl-, 1-phenyl-3-butynyl ester (9CI) (CA INDEX NAME)



09/701,893

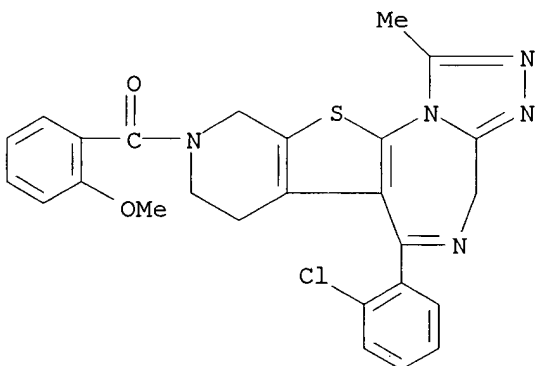
RN 140167-27-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl-9-[1-oxo-3-(2-pyridinyl)-2-
propenyl]- (9CI) (CA INDEX NAME)



RN 140167-28-8 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-7,8,9,10-tetrahydro-9-(2-methoxybenzoyl)-1-methyl-
(9CI) (CA INDEX NAME)



Wuuu

IT 130310-54-2 130335-42-1

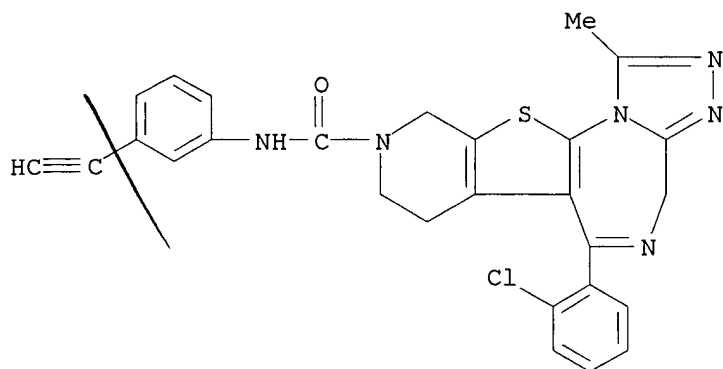
RL: RCT (Reactant)

(platelet-activating, factor antagonistic activity of)

RN 130310-54-2 CAPLUS

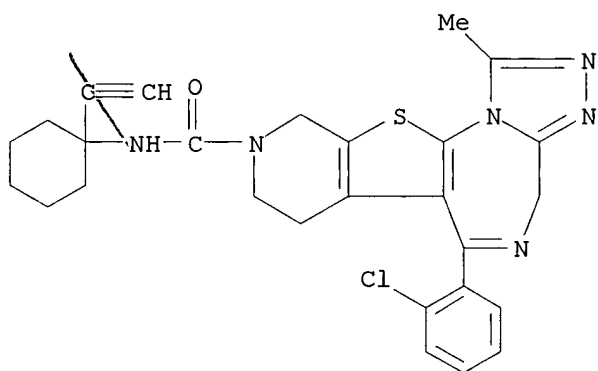
CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-
9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(3-ethynylphenyl)-7,10-dihydro-1-
methyl- (9CI) (CA INDEX NAME)

09/701,893



RN 130335-42-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-N-(1-ethynylcyclohexyl)-7,10-dihydro-1-methyl- (9CI) (CA INDEX NAME)



IT 130312-25-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation of, with cyclopropionyl chloride)

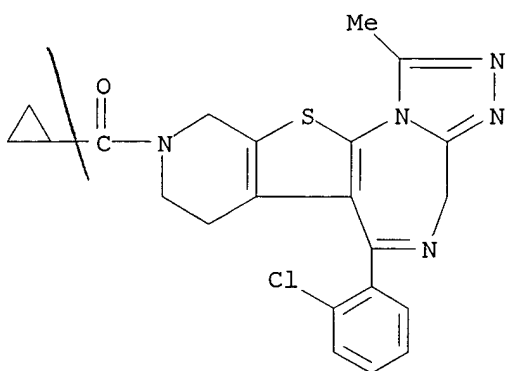
RN 130312-25-3 CAPLUS

IT 130310-39-3P 130311-20-5P

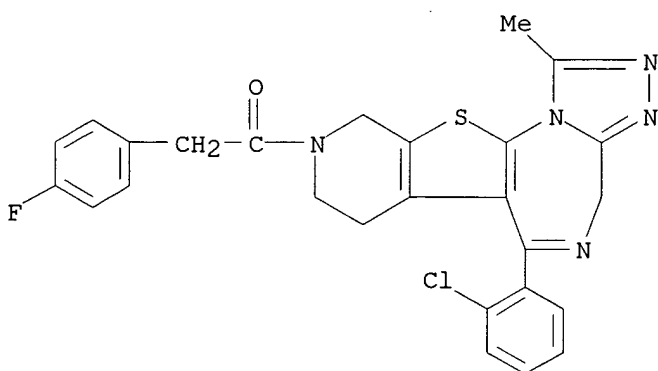
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and platelet-activating factor antagonistic activity of)

RN 130310-39-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



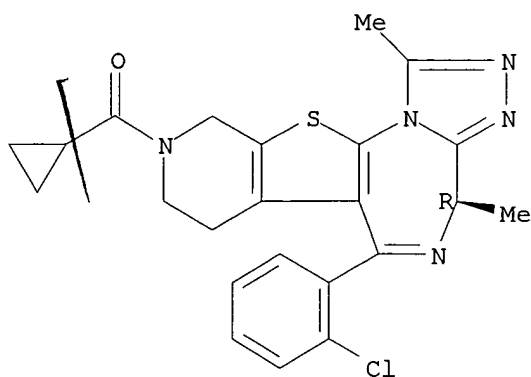
RN 130311-20-5 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-[(4-fluorophenyl)acetyl]-7,8,9,10-tetrahydro-1-methyl-
 (9CI) (CA INDEX NAME)



IT 130311-02-3P 131614-02-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and platelet-activating factor inhibitory activity of)
 RN 130311-02-3 CAPLUS
 CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
 6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
 dimethyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

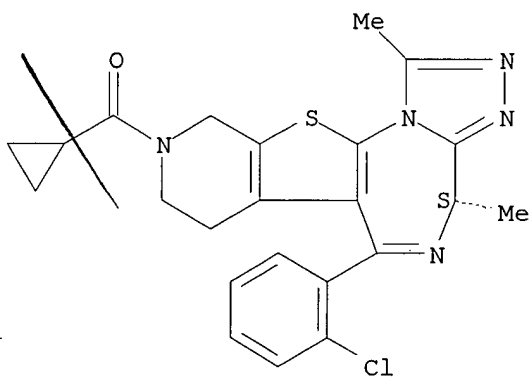
09/701,893



RN 131614-02-3 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine,
6-(2-chlorophenyl)-9-(cyclopropylcarbonyl)-7,8,9,10-tetrahydro-1,4-
dimethyl-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140224-77-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resolu. of)

RN 140224-77-7 CAPLUS

L23 ANSWER 23 OF 92 CAPLUS COPYRIGHT 2001 ACS

AN 1996:253280 CAPLUS

DN 124:331482

TI Determination of the anti-platelet-activating factor BN-50727 and metabolites in human urine by high-performance liquid chromatography using solid-phase extraction

AU Prunonosa, J.; Sola, J.; Peraire, C.; Pla, F.; Laverne, O.; Obach, R.

CS Pharmacokinetic Department, S. A. Lasa Laboratories, Barcelona, Spain

SO J. Chromatogr., B: Biomed. Appl. (1996), 677(2), 388-92

CODEN: JCBBEP; ISSN: 0378-4347

DT Journal

LA English

AB A sensitive and selective HPLC solid-phase extn. procedure was developed for the detn. of platelet-activating factor antagonist BN-50727 and its metabolites in human urine. The procedure consisted in a double solid-phase extn. of the urine samples on cyanopropyl and silica cartridges, followed by an automated solid-phase extn. of the drug and metabolites on CBA cartridges and posterior elution online to the chromatog. system for its sepn. The method allowed quantitation in the concn. range 10-2400 ng/mL urine for both BN-50727 and the main metabolite, the O-demethylated BN-50727 product. The limit of quantitation for both compds. was 10 ng/mL. The inter-assay precision of the method, expressed as relative std. deviation, ranged from 1.9 to 4.5% for BN-50727 and from 2.5 to 9.0% for the metabolite. The accuracy, expressed as relative error, ranged from -2.4 to 4.2% and from 0.2 to 6.2%, resp. This paper describes the validation of the anal. methodol. for the detn. of BN-50727 in human urine and also for its metabolites. The method has been used to follow the time course of BN-50727 and its metabolites in human urine after single-dose administration.

IT 114800-58-7, NHPTT 132418-35-0, BN-50727

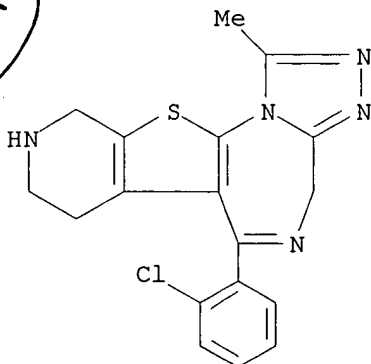
165898-01-1

RL: ANT (Analyte); ANST (Analytical study)

(detn. of anti-platelet-activating factor BN-50727 and metabolites in human urine by high-performance liq. chromatog. using solid-phase extn.)

RN 114800-58-7 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine, 6-(2-chlorophenyl)-7,8,9,10-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)

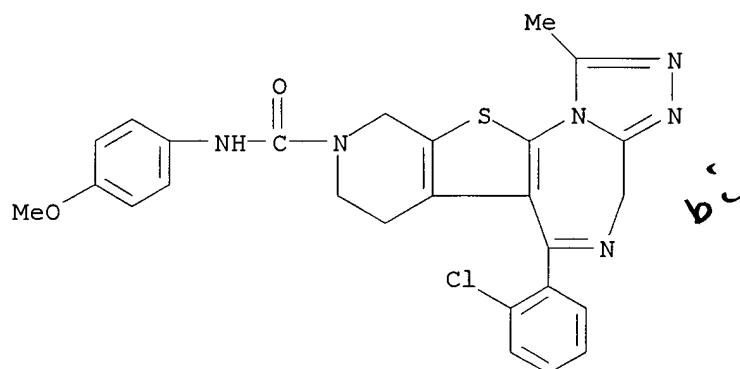


RN 132418-35-0 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-methoxyphenyl)-1-

09/701,893

methyl- (9CI) (CA INDEX NAME)



RN 165898-01-1 CAPLUS

CN 4H-Pyrido[4',3':4,5]thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-9(8H)-carboxamide, 6-(2-chlorophenyl)-7,10-dihydro-N-(4-hydroxyphenyl)-1-methyl- (9CI) (CA INDEX NAME)

